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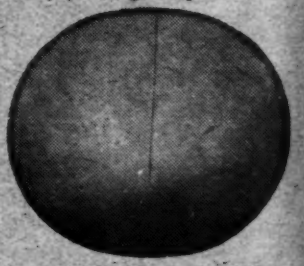

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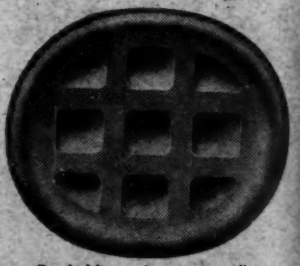

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 12 1951

FUNDAMENTAL PROBLEMS IN THE PATHOLOGY OF MULTIPLE SCLEROSIS AND ALLIED DEMYELINATING DISEASES*

BY

C. E. LUMSDEN, M.D.

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[WITH PHOTOGRAVURE PLATE]

In 1868 appeared Charcot's original description of the histology of multiple sclerosis. Out of the 82 years of unremitting research since then has emerged a conviction that this disease is not caused by any single infective or single extrinsic toxic agent but that, along with the other primary demyelinating diseases, it has its causation in some more complex intrinsic biological disturbance within the highly specialized myelin sheaths which insulate most of the conducting apparatus of the brain and spinal cord. It is not my intention to deal with the research, which has been entirely unsuccessful after several false trails had been followed, done in the attempt to show transmissibility of multiple sclerosis; this has been fully reviewed elsewhere, notably by Brain (1930) and by Schaltenbrand (1943).

With regard to the other theories of their causation, the 660-page volume, *Multiple Sclerosis and the Allied Demyelinating Diseases*, published this year by the Multiple Sclerosis Commission of the American Association for Research in Nervous and Mental Diseases, provides a fairly comprehensive bibliography. In addition to this volume, and to Schaltenbrand's monograph, there have in recent years been several interesting shorter papers of a review character such as those of Moreau (1932), McAlpine (1946), van Bogaert (1947), and, on experimental aspects, that of Hurst (1944). No such review is therefore necessary here, and it is my purpose simply to deal with some of the problems that appear to me from the standpoint of experimental pathology to be fundamental.

The term "demyelinating disease" applies to those conditions in which myelin sheaths are primarily destroyed but the axons and neurone bodies are largely spared, although to a variable degree in the individual disease. By common usage, in this group, in man, are multiple sclerosis and the diffuse demyelinating diseases, including neuromyelitis optica and the concentric sclerosis of von Baló, of which latter disease Hallervorden and Spatz (1933) have given a most interesting account, with special regard to the physical and chemical factors thought to be concerned in the spread of this process. On debatable frontiers lie three groups of conditions in which myelin is also, but to a much more limited extent, specifically involved—namely, in (*a*) acute disseminated leucoencephalopathies occasionally complicating the exanthematous and certain other fevers; (*b*) subacute combined degeneration of the cord; and (*c*) certain metabolic disorders such as the lipodystrophies and phenylpyruvic oligophrenia.

In animals, also, several demyelinating disorders, possibly of different nutritional deficiency origins, occur notably amongst apes (Schroeder, 1908), monkeys (Levaditi *et al.*, 1933; van Bogaert, 1939), dogs (Perdrau and Pugh, 1930; Scherer and Collet, 1939), lambs (Bennetts and Chapman, 1937; Innes and Shearer, 1940), and horses (Hurst). While working in the Institut Bunge, Antwerp, I was able to study material on these conditions reported by van Bogaert and by Scherer, and I am also indebted to Dr. J. R. M. Innes and Dr. E. W. Hurst for the opportunity to examine some further material. Similar conditions, it should be added, have been reported also in foxes, moose, and goats (King and Meehan, 1948). By comparison with human material it is quite evident, however, that whatever their causes none of these animal diseases is exactly similar to multiple sclerosis. It may therefore be important to consider whether multiple sclerosis is a specific form of reaction on the part of the human brain. For this reason it might be that even if, for the sake of argument, we found the cause of multiple sclerosis to be a specific transmissible agent, animate or inanimate, it might not be capable of evoking the lesions of multiple sclerosis in animals. Even negative experimental results will therefore have to be scrutinized with care.

Encephalitis Periaxialis Diffusa

In man "encephalitis periaxialis diffusa," separated out from the diffuse scleroses by Schilder (1912), is itself a heterogeneous group of conditions. Einarson and Neel have proposed the present classification: (1) glioblastomatous reactive type; (2) inflammatory reactive type; (3) sporadic degenerative type: (*a*) with metachromatic prelipoids, and (*b*) with both fatty and metachromatic lipoids; and (4) familial heredodegenerative type, subdivided into: (*a*) acute infantile form (Krabbe, 1916), (*b*) subacute juvenile form (Scholz, 1925), (*c*) adult form (Ferraro, 1927), and (*d*) chronic "Pelizaeus–Merzbacher" form.

In the main this classification is approved by Greenfield (1950), except for the glioblastomatous type, which most neuropathologists agree should be excluded, for

*Florence Tong Lecture delivered to the Association of British Neurologists at the National Hospital, Queen Square, London, on December 16, 1950.

the reason that, with the modern improved identification of the gliomata, it has become evident that the glioblastomatous form of demyelinating disease is simply an expression of a diffusely infiltrating glioma with secondary demyelination such as can occur from associated oedema (Greenfield, 1939).

Of the other varieties in the present list I have examined material altogether from 23 cases: three were original, and the others, studied at the Salpêtrière and at the Institut Bunge, were mainly from among cases already reported from these laboratories.

The most striking impression one gains is that of the wide range of histochemical differences from case to case amongst the "degenerative" type, whether of familial or of sporadic nature. In this degenerative group of cases, including those with different grades of "prelipoid" substances, those with true metachromatic substances, those with mucinoid change in the oligodendroglia, and other variants such as Collier and Greenfield's (1924) type with "globoid" cells, there is a wide spectrum indeed.

Continental workers call these "heredo-degenerative" types *leucodystrophy*, a strictly accurate and certainly useful term to distinguish them from the classical type of Schilder's own Case 1. It does not always seem to be clearly appreciated in the literature that Schilder himself described under the name "encephalitis periaxialis diffusa" three quite different types of cases:

1. The 1912 case, in a girl aged 14, was the now classical form with a giant plaque of demyelination and sclerosis with sharply punched-out contours, occupying asymmetrically a large part only of each hemisphere. There were a few other discrete demyelinating lesions elsewhere in the brain and brain-stem, and Schilder thought that the condition might be a childhood variant of multiple sclerosis.

2. His second (1913) was a redescription of a case reported previously by Haberfeld and Spieler (1910). This was familial. It corresponded much more to the classical familial variety in which the whole of the neoencephalic myelin is affected even into cortex, and it was characterized by a dense accumulation of "prelipoid" substance.

3. The third case, reported in 1924, presented a different picture altogether, as Schilder recognized. It occurred in a woman aged 37 one month after influenza. A study of his report now suggests that the condition had much more in common with van Bogaert's (1945) subacute sclerosing leucoencephalitis than with either of Schilder's earlier cases.

A Variable Feature

Those cases of diffuse sclerosis of the type similar to Schilder's Case 1 are the preponderating type, and in contrast to the structural and histochemical variations in the leucodystrophies they show a remarkable uniformity in their basic features. Their only variable feature is in the location of the large plaque. The fact that in Bouman's (1934) well-known monograph, *Diffuse Sclerosis*, four out of five cases examined post mortem showed lesions of this plaque-like form served to perpetuate the misapprehension of the unity of Schilder's "encephalitis periaxialis diffusa," when the more logical assumption would now seem to be that this form, like Schilder's Case 1 on the one hand and the heredo-degenerative or leucodystrophic forms on the other, is fundamentally different.

We have seen that in Schilder's own Case 1 the giant plaque was not the only lesion present. Scrutiny of the literature shows that this multiplicity of lesions is often described. Bouman recognized the existence of "polysclerotic" forms, and finally Heernu, Martin, and van

LEGENDS TO PLATE

Figs. 1 to 8 illustrate some of the main features discussed of "encephalitis periaxialis diffusa," and Figs. 9 to 13 show some of the main aspects of classical and acute multiple sclerosis. Figs. 15 and 16 allow comparison of the naturally occurring post-vaccinal encephalomyelitis of man and the experimental "allergic" encephalomyelitis of lower mammals. Fig. 14 is from a living oligodendroglial cell.

FIGS. 1–3.—Leucodystrophy. Formalin-fixed brain of 4-year-old child. Frontal, central, and parietal levels respectively. Note the transparent moiré appearance of the white matter due to the absence of myelin, except in the lower parts of the pyramidal tracts passing down into the crura of the mid-brain.

FIG. 4.—Same case as in Figs. 1–3. Giant paraffin section at level of Fig. 2. Stained by Loyez's method for myelin (black). This confirms the absence of myelin except in region of thalamus and crura cerebri.

Figs. 5–6.—Another case of leucodystrophy. Fig. 5 is a coronal section taken at level of posterior horn of lateral ventricle. There is residual myelin in the tapetal zone. In this case there is diffuse demyelination also in the cerebellum (Fig. 6). Myelin preparations.

FIG. 7.—"Prelipoids" from a case of familial leucodystrophy. The section is stained for myelin, which has disappeared from the nerve-fibre sheaths and now occurs as coarse masses, up to 50 μ in diameter. On the left some of it has been engulfed by phagocytes (the smaller spherical masses seen in the vicinity of a blood vessel—i.e., towards the left of the picture) (× 60 approx.).

FIG. 8.—"Encephalitis periaxialis diffusa" of the type of Schilder's classical Case 1. The lesion is a giant plaque of demyelination with sharply punched-out contours. The cavity seen in the centre of the gyrus at the bottom right corner is due to loss of the thin friable tissue during technical handling. Speilmeyer's method for myelin.

FIG. 9.—Multiple sclerosis. Two typical plaques in periventricular white matter (ventricle, left middle). Note the sharply cut-out edges of the plaques but without swelling, shrinkage, or tissue loss. Loyez's stain for myelin (black). Slightly enlarged.

FIG. 10.—Early multiple sclerosis. Two "shadow plaques" in the white matter (staining black). The white arcuate zones to the left, top, and right are unstained cortex.

FIG. 11.—Typical multiple sclerosis plaque round a small vein, seen (on the right side) immediately subcortically. Unstained, formalin-fixed, slice of brain (× 2 approx.).

FIG. 12.—Microscopical view of edge of a typical multiple sclerosis plaque showing abrupt delimitation of the process with the absence of breakdown of the ground substance. Loyez's iron-haematoxylin for myelin (black) (× 60 approx.). The small scattered black elements in the demyelinated region are cell nuclei and erythrocytes in the lumina of blood capillaries.

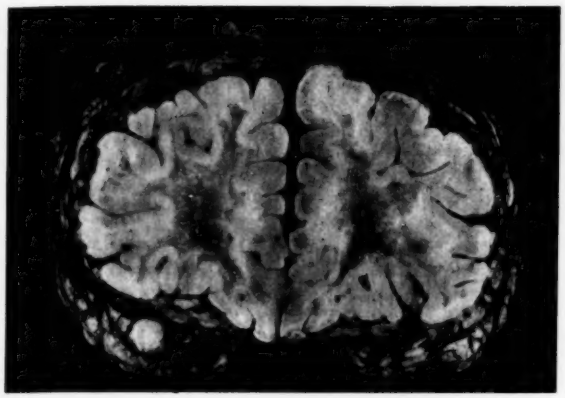
FIG. 13.—Acute multiple sclerosis. Dr. van Bogaert's case (see text). Numerous sharply defined shadow plaques (grey) seen in the white matter (stained black). The small oval white lumina are spaces left where the thin-walled veins, cut in cross-section, have fallen out of the preparation.

FIG. 14.—Living oligodendroglial cell in tissue culture. Photographed under phase-contrast (× 400). For description, see text.

FIG. 15.—Post-vaccinal encephalomyelitis in man. Loyez's stain for myelin (× 60). Showing the halo of cellularity and "myelinoclasis" around small vein, seen cut across four times in this plane. The lumen of the vein is black owing to staining of the contained erythrocytes by the method.

FIG. 16.—Experimental "allergic" encephalomyelitis in guinea-pig brain. Same stain and same magnification as Fig. 15. See text.

C. E. LUMSDEN: MULTIPLE SCLEROSIS AND DEMYELINATING DISEASES



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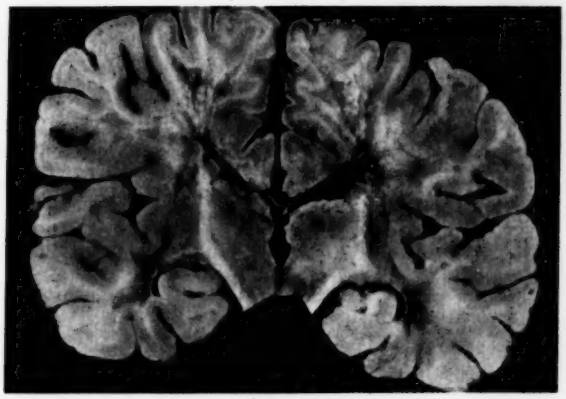

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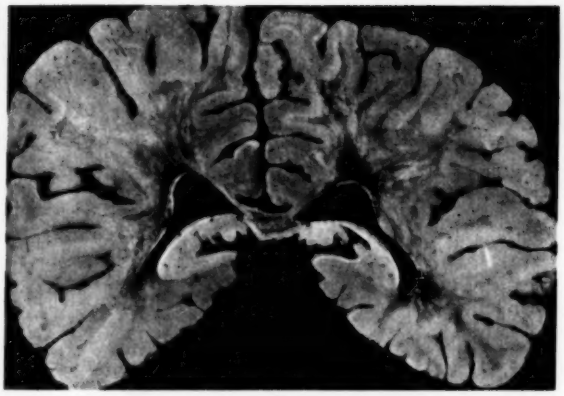

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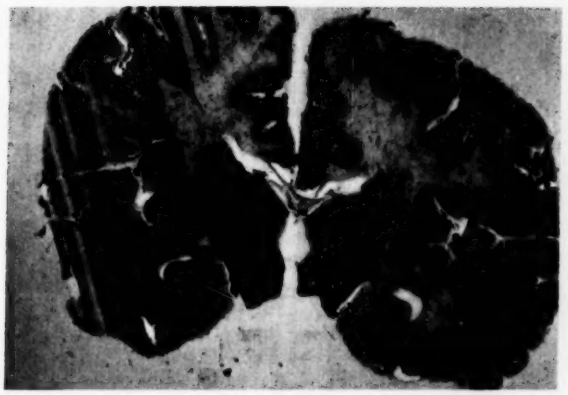

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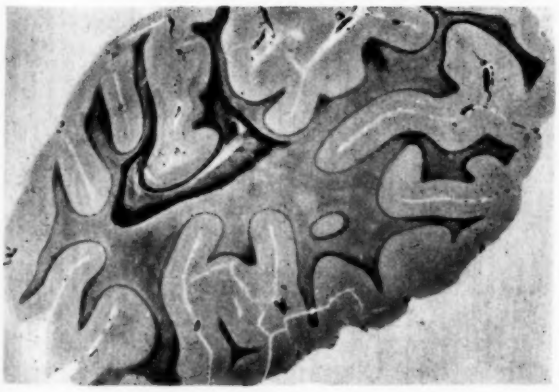

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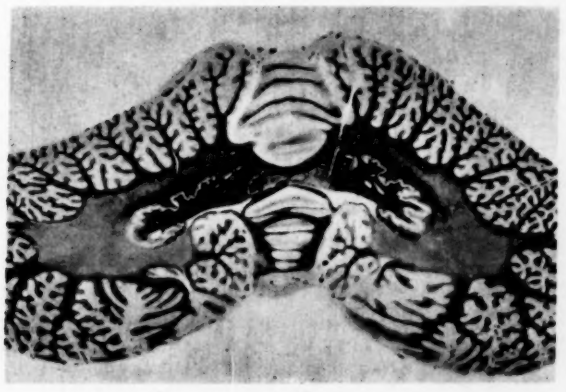

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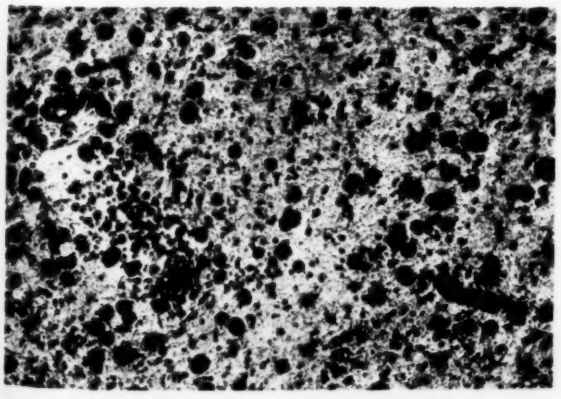

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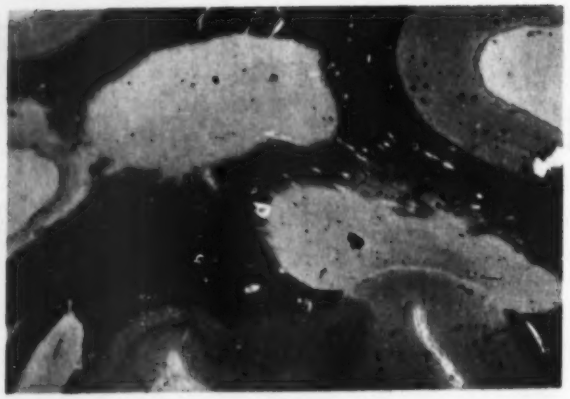

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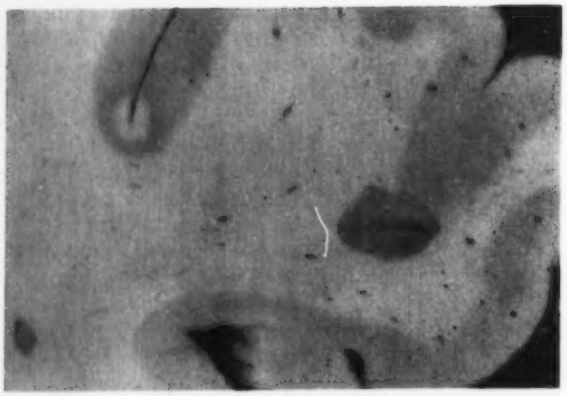

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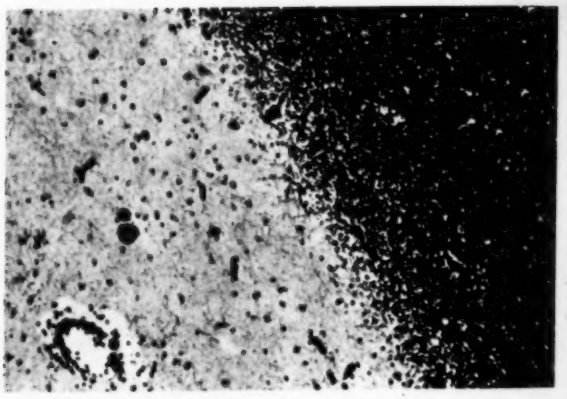

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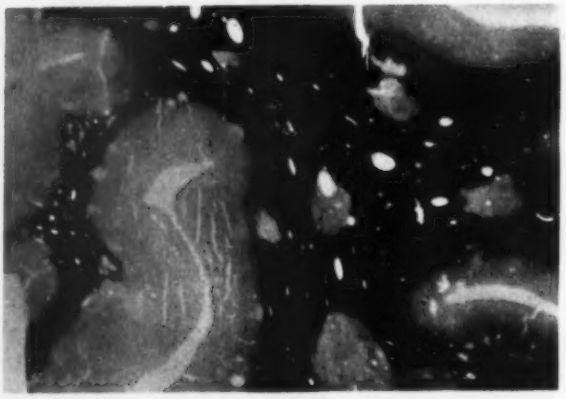

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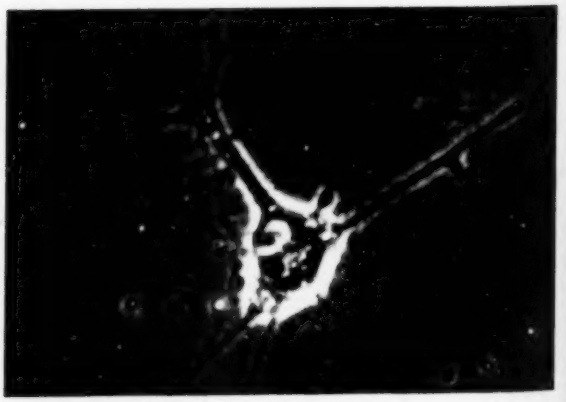

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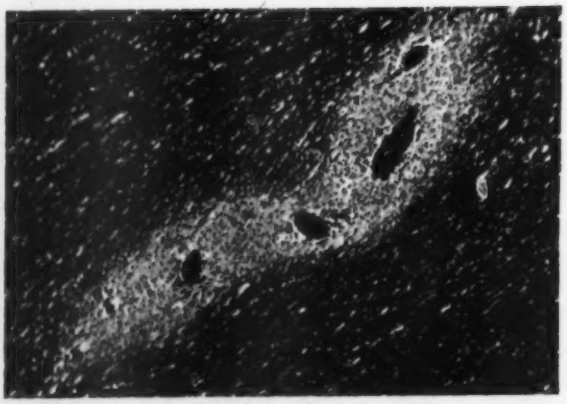

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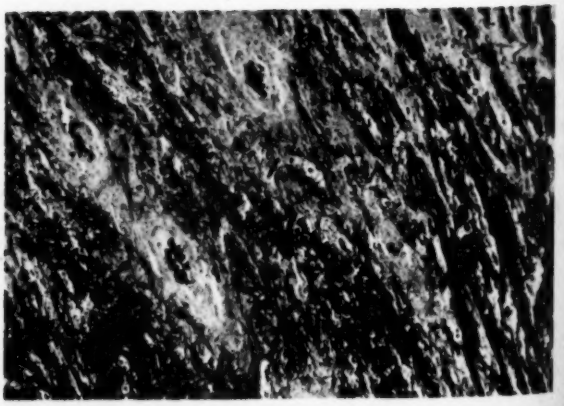

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Bogaert (1945) produced conclusive evidence that there is no real anatomical distinction between Schilder's disease of his classical Case 1 type and multiple sclerosis. Amongst the intermediate forms are Devic's neuromyelitis optica, von Baló's concentric sclerosis, and another variety which Greenfield (1950) has added—namely, a demyelinating myelopathy with a coincident diffuse demyelination of one occipital lobe.

In summary, then, there are in fact really only two varieties of true primary demyelinating disease in man: (1) the leucodystrophies, and (2) multiple sclerosis, with, as a variant, diffuse sclerosis of the type of Schilder's Case 1.

The Leucodystrophies

The most remarkable structural feature of the leucodystrophies is the high frequency with which "prelipoid" substances, and products staining metachromatically with basic aniline dyes, are present. The "metachromatic leucoencephalopathies" have been the subject of several interesting papers recently by van Bogaert and Dewulf (1939), Einarson and Neel (1938, 1940, 1942), Einarson *et al.* (1944), Norman (1947), and Greenfield (1950); but the relationship to those of older cases in the literature which were characterized by masses of tinctorially abnormal prelipoids, such as the cases of van Bogaert and Scholz (1932), of Scholz (1933), and of van Bogaert and Bertrand (1933), has never been formulated.

It is now evident, however, that, since attention has been drawn to this feature of metachromasia, more and more, and perhaps all, of the familial cases show this abnormal accumulation of higher lipoids in variable degree, as well as the "sporadic" forms of leucodystrophy. It is well to remember that cases classified under the "sporadic" group undoubtedly include many cases of only children, so the distinction between "familial" and "sporadic" forms is just not valid. Further, metachromatic prelipoids are not necessarily limited to diffuse forms of leucoencephalopathy. For instance, Guillain, Bertrand, and Gruner (1941) have described under the title "leucoencéphalite à nodules morulés gliogènes" a most interesting case in which clusters of cells like Greenfield's "globoid" cells containing metachromatic prelipoid were present in two discrete symmetrical foci in the white matter of the putamina.

That the oligodendroglia is especially affected was first suspected by Collier and Greenfield in 1924 in a case which later proved to be familial. They proposed that the primary attack in diffuse demyelinating disease is "upon those cells that have to do with the nutrition of myelin." This view was also expressed by del Rio Hortega in 1928. Since that time Greenfield (1933) has separated out as a special variety those forms in which the affection of the oligodendroglia seemed particularly marked. The occurrence of metachromatic substances in the so-called "mucinoid degeneration of the oligodendrocyte" as well as the freely occurring prelipoid in the leucodystrophies suggest a close relationship in the metabolism of myelin and of the cytoplasmic constituents of the oligodendrocyte. As metachromasia seems to be due to polysaccharide constituents within cells it may be postulated for the moment that the metachromatic substances present in the leucodystrophies are, or are related to, galactosphingosides or cerebrosides, and that the oligodendrocyte is intimately concerned with the metabolism of these substances, which indeed may be the main energy source of this cell. We shall see the possible importance of this when discussing the physiology of this cell later.

Meanwhile it should be noted that Norman (1947) has emphasized that in these leucoencephalopathies the metachromatic substances are not limited to the central nervous system but have been found also in renal tubular epithelium, in liver, gall-bladder, pituitary, and testis—evidence indicating that these diseases are not limited to brain myelin but that they bear kinship with the general lipoidoses. In support of this, attention has been drawn to the widespread arrest of myelination in early cases of Tay–Sachs's disease (Norman), in Niemann–Pick's disease (Bertrand and van Bogaert, 1934), in Gaucher's disease, and in xanthomatosis both of the Schüller–Christian type (Davison, 1942; Globus, 1942), and of the curious type described as "cerebral cholesterolinosis" by van Bogaert, Scherer, and Epstein (1937).

Throughout all of these general lipoidoses there is the same individual variation from case to case in the distribution of the stored lipoid within the various organs as we have seen occurs in different elements of the nervous system as well as in other organs in the instance of the leucodystrophies. Yet the sphingomyelin in Niemann–Pick's disease, the kerasin in Gaucher's disease, and the cholesterol in xanthomatosis appear from such analytical studies as have been made (Sobotka, 1942; Sperry, 1942) to show no qualitative difference from those normally metabolized. Nor has any increase of these lipoids been found in the blood stream in cases of Gaucher's, Niemann–Pick's, and Tay–Sachs's disease (Thannhauser and Schmidt, 1946).

It is apparent that it is not so much with abnormal lipoid or with an excessive supply in the blood plasma that we are dealing, but that it is *the rate of their metabolism* within the affected cells which is impaired. And the wide range of difference in the histological distribution of the lipoids from case to case indicates, further, that this defect resides in individual cells and not in any general chemical disturbance within the circulating fluids. In other words, the "metabolic abnormality" which is commonly taken to be present is not an abnormality of the lipoid substrates but of the intracellular mechanisms—that is, enzymes—concerned in the utilization of these substrates for the immediate purposes of the cell and its processes. In this regard it should be noted that studies with the stable isotope deuterium (Sperry and Waelsch, 1950) have confirmed that these brain lipids, even in the adult, are in a state of constant metabolic turnover or "dynamic equilibrium."

Multiple Sclerosis

It is important to note that, although the disease is only of sparsely scattered incidence anywhere in the world (up to about 50 cases per 100,000 of population), there seems to be a significantly great geographical variation, as McAlpine (1946), Limburg (1950), and Kolb (1950) have severally indicated. Mortality statistics show no selective association between multiple sclerosis and population density, however. Nor are seasonal variations in onset and recurrence of and death from the disease statistically significant, so that there is no real support here for an infective theory. There is no evidence of any racial factor. It would appear, therefore, that the variation is in some way due to a geological or climatological factor, including, of course, a nutritional element.

In the histopathology of the disease my own experience is based on the examination, in various centres, of some 60 cases, 15 of which have been reported in some detail elsewhere (Lumsden, 1948).

Characteristic Lesions

The characteristic lesions of multiple sclerosis are confined to the central nervous system, including the optic pathways. The intrathecal portions of the cranial nerves and of the anterior and posterior spinal roots may occasionally be involved at their origins if in immediate contiguity with plaques within the brain substance, but discrete plaques are never seen. The extravertebral portions of the roots and the peripheral nerves are never involved by plaques, though non-specific varieties of neuritic change have been described sometimes, notably by Hassin (1921) and Schaltenbrand (1943). In two instances only, to my knowledge, have plaques been seen in posterior root ganglia. As these structures contain oligodendrogliocytes, these two instances provide no exception to the general rule that multiple sclerosis plaques are found only where oligodendroglia exists.

The classical lesions within the central nervous system are the widely disseminated discrete plaques of demyelination and gliosis with the characteristically sharply punched-out contours. Such plaques appear to grow by spreading in diameter, preferentially in the white matter, though not infrequently encroaching upon the grey. They may coalesce to form larger lesions, which may, for instance, cover almost the entire cross-sectional area of the spinal cord, with, it is noted, often disproportionately little functional result. Their contours show no evident tendency to be delimited by blood vessels or by pial septa.

Equally peculiar to multiple sclerosis are the true shadow-plaques, or *Markschattenherde*, where demyelination is only partial—but evenly so—throughout the plaque, and where the same sharply punched-out character of the contours is still preserved. With Kultschitsky's haematoxylin they look like an ink-stain blotted while still wet. Their real nature has been a mystery, but the recent studies on the normal myelin that have been made with *x*-ray diffraction and electron microscopical methods appear to me to suggest an explanation. Schmitt's (Schmitt *et al.*, 1941) work has shown that the lipid molecules in the sheath are arranged with their long hydrocarbon chains extending radially and are laid in concentric layers alternating with neurokeratin. Each lipid–protein layer measures 186 Å and contains 25 Å of water molecules—that is, some 13%. This figure falls short of the chemically realizable water content, which varies from 35 to 50%. To explain the difference it was predicted by Schmitt that there are periodic water channels breaking the myelin into concentric layers. Electron microscopical studies by Fernández-Morán (1950) have confirmed the existence of such myelin lamellae. I believe that the shadow-plaques of multiple sclerosis may be due either to decortication of the outer myelin lamellae or to imbibition of water molecules into the interlamellar channels, and that it should easily enough be possible to elucidate this with one of these two ultraphysical methods.

It is an old controversy, indeed, whether the plaques are centred round blood vessels or related to vascular territories. The failure of Putnam's thrombosis theory of multiple sclerosis to gain acceptance has tended to prejudice some neuropathologists against the view that any vascular factor is concerned in the genesis of the disease. But in my experience it is indisputable that plaques are *sometimes* centred round veins and venules, particularly in the acute lesions, in such a way as to suggest a more than fortuitous relationship. In most chronic lesions no such perivascular relationship is evident, but the marked tendency to a subependymal distribution of plaques may be due to some relationship with the venous drainage rather than with any intrinsic association with the ventricular fluid. In the same way the distribution of plaques in the spinal cord often suggests a relationship to the venous territories (Fog, 1950).

The microscopical characteristic of the multiple sclerosis plaque is the suddenly delimited demyelination with complete or relative preservation of the axis cylinders—the *dissociation axomyélinique* of the Continental authors—with the laying down of parallel strands of neuroglial fibres alongside the intact axons, a physical structure which is probably the main explanation of the characteristic translucency of plaques.

"Secondary Demyelinations"

Of course, other conditions from time to time mimic plaques of multiple sclerosis. These secondary demyelinations occur in a formidable array of diseases, including the toxic encephalopathies of hepatic disease (Crandall and Weil, 1933; Baker, 1949), uraemia (Hechst, 1932; Hiller and Michalovici, 1941; Knutson and Baker, 1945), eclampsia (Schmorl, 1902; Diamond, 1936), dysentery (Spielmeyer, 1922), and porphyria (Baker and Watson, 1945); in the primarily anoxic encephalopathies associated with chronic cyanotic heart disease, anaemias like pernicious anaemia (Lurie, 1919; Lebensart, 1934), the local anoxic complications of cerebral malaria (Rigdon, 1944), and the cerebral vascular complications of rheumatism (Costero, 1949). In the same category belong the experimental microembolic and microthrombotic lesions which I have reported elsewhere (Lumsden, 1950), as well as the so-called "demyelinating" lesions caused by oedema around tumours such as Greenfield (1939) has reported. In individual lesions there may very occasionally be some difficulty in distinguishing such "*plaques simulatrices*" from plaques of multiple sclerosis, especially when this latter is associated with some axonic damage and secondary Wallerian change, as one must admit can sometimes occur in the necrotizing forms. But the important thing is the overall character of the lesions.

On the basis of the generally accepted histopathological criteria, multiple sclerosis could now be defined as follows: a process affecting nerve fibres within the central nervous system, with the production of focal lesions which are disseminated and which continue to evolve slowly and often intermittently to the formation of sclerotic plaques in which the axis cylinders are largely preserved. The process remains predominantly periaxial and discontinuous, thus producing plaques of demyelination characterized by abrupt contours which extend eccentrically and irregularly through the myelinated parenchyma. Any of the individual criteria in this definition can be fulfilled singly or in groups by other conditions, but, taken together, they delineate a disease process that embraces all cases of classical multiple sclerosis and excludes all other conditions.

I deal later with the more debatable "acute" or initial forms of the disease, but even on the most

generous estimate these have not exceeded 5 or 6% of the total in any large number of cases of multiple sclerosis studied pathologically. It is the entitative character, then, of the 95% of classical multiple sclerosis that has to be explained by any acceptable hypothesis of causation. Far from reproducing this entitative character in 95% of the lesions they cause, the agencies so far blamed for multiple sclerosis—such as spirochaetes and neurotropic viruses (e.g., Bailey *et al.*, 1949), thrombosis (Putnam, 1933, 1935, 1937; Putnam and Alexander, 1939), or lead-poisoning (Campbell *et al.*, 1950)—can only very rarely produce any lesions which even mimic multiple sclerosis.

Broadly, then, the contribution of structural pathology to the problem of the causation of multiple sclerosis has been to narrow the field to a choice of two views: either (1) if the real cause is a specific transmissible agent it must be a virus or a chemical substance not yet even listed amongst the known pathogenic agents, and one with some extremely uncommon properties; or (2), alternatively, the disease may be only a specific form of reaction on the part of the nervous system peculiar to certain individuals and, within limits, independent of its immediate precipitating cause.

Role of the Oligodendrocyte

On the significance of non-parenchymal reaction in the brain in multiple sclerosis there has been no controversy since the Strümpell–Müller hypothesis of "dysplastic glia development" was dropped and argument subsided on the "degenerative" or "inflammatory" significance of the perivascular round-cell reaction that may be associated with the lesions. In one important respect, however, this field has been completely neglected—namely, concerning the role and fate of the oligodendroglia in multiple sclerosis. A study of my own material showed a complete loss of this cell from the plaques of demyelination both in the acute and in the chronic lesions. The oligodendrocytes disappear as abruptly as the myelin sheaths, but this is equally true in secondary demyelinating conditions. In the grey matter local reactive proliferation of perineuronal oligodendrocytes certainly occurs in syphilitic and other types of polio-encephalitis, but in the white matter the reactive potentialities of the interfascicular oligodendroglia, for instance in rheumatic lesions, is indeed limited and short-lived. This cell undergoes extremely rapid autolysis post mortem, and no cytochemical research has in consequence been so far possible on it in human material.

Perhaps the solution of the whole obscure problem of the demyelinating diseases may prove to be in the biology of the oligodendrocyte. We already know much about the biology of the neurone, its chemistry, its bioelectric phenomena, its mode of growth in culture, and the way it is affected by pathological agencies; and we know something likewise of these aspects of the astrocyte and microgliocyte. Concerning the oligodendrocyte, the most numerous cell within the central nervous system, we know strictly nothing of its role in health and disease apart from the general assumption, attributable mainly to its discoverer, del Rio Hortega (1921, 1928), that it is in some way concerned in the maintenance of the myelin sheaths.

The claim by Canti, Bland, and Russell (1935) to have grown cells from two cases of oligodendroglioma in the human subject suggested to me that it might be possible likewise to grow the normal oligodendrocyte or at least to maintain it alive in tissue culture for a period of some few days, during which its vital phenomena could be observed. Corpus callosum of the normal healthy adult rat provided explants in which the nucleated cells were almost entirely oligodendroglial. The details of the methods used and observations made are reported elsewhere (Lumsden and Pomerat, 1951).

Briefly, these cells appear in clusters at the margin of the explant, chained together by long filamentous processes, usually four or five per cell, with highly amoeboid terminal expansions. When studied in cinematographic records these oligodendrocytes are seen to exhibit a remarkably strong rhythmic contractility quite unlike the movements of astrocytes and microgliocytes of nervous tissue on the one hand, or fibroblasts, macrophages, and other mesodermal elements on the other. Because of their interconnecting processes these contracting cells engage in a curious and highly characteristic continual tug-of-war. The whole contraction phase of each cell takes about five minutes and consists of a shorter contraction phase, systole-like, lasting one and a half minutes, and a more prolonged expansion phase, diastole-like, lasting about three minutes.

With such preparations it should be possible now to investigate many problems. With the special microirrigation chambers (which already exist for this type of work in tissue-culture laboratories) it would be simple to examine the reaction of living oligodendrocytes to various potential "toxins" such as extracts of multiple sclerosis plaques, comparing these with normal brain from the same and also from a healthy subject. Sera from animals with experimental "allergic" encephalomyelitis, and dilute solutions of salts of trace elements like copper or lead such as have been thought to play a part, favourable or adverse to the patient, in the genesis of multiple sclerosis, could be assayed similarly. Furthermore, with these cells, which have such a remarkably rhythmic contractility, electrical phenomena likely to be associated with the contraction can, we hope, soon be studied directly. What effect such electrical changes might have on the normal electroencephalogram offers fascinating material for speculation.

The Initial Lesions

One of the difficulties in understanding the pathology of multiple sclerosis is that, because of the insidious character of the disease, we do not really know what the initial lesions are like. One school of neuropathologists, including Hassin (1921, 1937) and Spielmeyer (1930, 1931), has held that the lesions are always of the classical type from the outset. The opponent school has maintained that they begin as an acute disseminated encephalomyelitis. There are a few cases on record in which death occurred from some incidental cause during the earliest phases of multiple sclerosis. A most valuable case of this type is one reported by Cournand (1930). I had the opportunity of examining the material from this case at the Salpêtrière. Here the lesions, though apparently no more than a few weeks old, even histopathologically, already bear the stamp of indubitable multiple sclerosis.

If, on the other hand, we take a subacute case of post-vaccinal encephalitis for direct comparison—such as a most interesting case (Case XII), with survival for

108 days, as reported in Blackwood's (1944) Edinburgh series—we find that the encephalomyelitis heals by the ordinary processes of glial and mesodermal scarring and shows no resemblance whatsoever to incipient multiple sclerosis. Furthermore, some hundreds of non-fatal cases of acute disseminated encephalomyelitis of the post-exanthematous type have now been followed over a sufficient number of years (Kudelka, 1932; Kaiser and Zappert, 1937) to show that at least this variety never progresses to multiple sclerosis even though it is the commonest form of acute disseminated encephalomyelitis and the one which pathologically, by reason of its "myelinoclases" or partial softening of the white parenchyma, most nearly imitates multiple sclerosis.

It would appear, therefore, on the evidence I have outlined, that multiple sclerosis and acute disseminated encephalomyelitis are different diseases from the outset.

Reference must be made here, however, to a unique case in my experience—namely, that reported by van Bogaert from Spielmeyer's laboratory in 1932.

A 12-year-old girl died of an acute febrile cerebral affection 18 days after the appearance of a typical varicellar rash. The brain showed an acute disseminated encephalomyelitis with punched-out foci of demyelination scattered like oil-drops within the white matter. The lesions are uncannily like multiple sclerosis, a fact which Spielmeyer himself admitted, while none the less regarding acute multiple sclerosis and acute disseminated encephalomyelitis as different diseases.

It is untenable that in this case we have two processes fortuitously associated. Is this, then, the unique case upon which, after all, we are to conclude that multiple sclerosis begins as acute disseminated encephalomyelitis? Surely not. If this were so, most multiple sclerotics would have a history suggestive of acute disseminated encephalomyelitis, and most non-fatal cases of acute disseminated encephalomyelitis would evolve to multiple sclerosis. This does not happen. Therefore it seems we must accept this compromise: that, while they are different diseases, in very rare cases multiple sclerosis may arise from acute disseminated encephalomyelitis which is merely *one* of the potential precipitating causes.

Experimental Encephalomyelitis

This problem of the relationship between multiple sclerosis and acute disseminated encephalomyelitis is no longer an academic one, for a form very similar to the latter disease in man can now readily be produced in animals by non-infectious means (Kabat *et al.* 1947; Morgan, 1947; Lumsden, 1949a, 1949b). This, the experimental so-called "allergic" encephalomyelitis, is a curious disorder that can be produced regularly in a high proportion of animals by a single subcutaneous injection, or a short series of injections, of sterile normal brain tissue from either homologous or heterologous species, suspended in an oily "adjuvant" base containing the products of killed tubercle bacilli. The disease can also be produced, though much less frequently or much more slowly, by the brain tissue alone without "adjuvants" (Rivers and Schwentker, 1935; Ferraro and Jervis, 1940).

"Adjuvants" alone and with killed tubercle bacilli will not themselves produce the condition; nor is the toxicity of the dead bacillus of any import, since harmless saprophytic varieties of acid-fast bacteria (Freund, Stern, and Pisani, 1947) serve equally well as a source of the enhancing substance, suspected to be a lipoid. The exact chemical nature of the enhancing agent, however, still remains to be shown, and how it operates—whether by conjugating itself with the active principle in the brain tissue or by evoking some preparatory cellular or humoral change in the body which sensitizes the brain of the injected animal to the brain tissue injected. The animal's own brain tissue removed by frontal lobectomy and injected subcutaneously will produce the lesion (Kabat *et al.*, 1949).

The possibility of a transmissible virus can be excluded, as neither prolonged autoclaving of the inoculum nor prolonged treatment with phenol or with strong formaldehyde solution destroys the encephalitogenic agent (Kabat *et al.*, 1948; Lumsden, 1949b). For these reasons, too, the agent is evidently not a protein. I have also reported that it is extractable with the myelin sheath lipoids sphingomyelin and cerebrosides and not with the axonic lipoids lecithin and cephalin (Lumsden, 1949b). The possibility of activation of a latent virus infection within the injected animals would seem to be excluded on the grounds of the high specificity of the inoculum and on the fact that the phenomenon is shown by a wide range of mammalian species tested—monkeys, guinea-pigs, rabbits, sheep, goats, and dogs—with an incidence rate diminishing in approximately that order from monkeys with a 90–95% susceptibility.

The disease produced in animals so inoculated is remarkably uniform throughout all species. The lesions consist of severe, disseminated, perivascular—essentially perivenular—partial softenings in the white matter, with a sharp microglial reaction and a proliferative response of the adventitial histiocytes in the vessel walls. Sometimes this latter element is very marked indeed and there is migration into the parenchymal territory on the part of these mesodermal elements so that a pseudogranulomatous lesion may develop. But, generally, such cellular emigration (including plasma cells and eosinophils) as occurs in some cases always appears subordinate to the general severity of the damage to the parenchyma. There is usually no capillaritis.

The perivenular partial softenings appear, of course, in myelin preparations as sleeves of demyelination, and several lesions may become confluent, so that widespread disintegration occurs within the centrum ovale. Even then, however, the neuroglial groundwork remains intact, so that no complete necrosis of the tissue is affected such as occurs, in contrast, in an infarct. Though the central veins and venules may be much engorged, there is no thrombosis. The degree to which the myelin is damaged varies with the animal species, monkeys showing considerably more demyelination than guinea-pigs and other animals. When, in the cases of remission with relapse which sometimes occur, opportunity is given to examine the late results of the lesion, these are seen to be glial and mesodermal scars and there is no evidence of production of any spreading demyelination at all comparable to multiple sclerosis.

If, then, this experimental disease does not reproduce multiple sclerosis, it has at least a remarkable similarity to acute disseminated encephalomyelitis of the post-exanthematous type in man. And somewhere there seems to be a tantalizing link with multiple sclerosis—for instance, in the distribution of the lesions especially in the optic pathways, and in the tendency to spontaneous remissions and relapses. The one thing

the experimental lesion lacks is any evidence of progressive spreading demyelination which is the so far unexplained peculiarity of multiple sclerosis.

When, therefore, we consider this experimental disease and its human counterpart, an obvious hypothesis presents itself—namely, that two disease mechanisms are concerned in multiple sclerosis: (1) a preparatory, exogenous mechanism which damages the white matter, and (2) an endogenous mechanism which liberates myelinolytic substance related to the myelin sheaths or the oligodendrocytes. With regard to the preparatory mechanism it may be that several different agencies act in this way. It may be that trauma, visceral tuberculosis, T.A.B. vaccination, diphtheria immunization, and other alleged precipitating causes which have been specifically incriminated in certain cases of plaque-like "Schilder's disease" in childhood, and that, in multiple sclerosis, lead and other toxic trace elements and the toxins of banal infections, as Pierre Marie maintained, may all be potential "trigger" causes which touch off the intrinsic mechanism which in susceptible individuals will lead to multiple sclerosis. To prevent the disease, our best hope, therefore, will be in some way to jam this exogenous "trigger" mechanism. Rational attempts to arrest the disease once initiated will involve methods designed to block the intrinsic mechanism.

Before concentrating on this latter aspect I would mention that in regard to the precipitating mechanism in the case of the experimental encephalomyelitis it has not yet been settled whether the encephalitogenic agency is really "allergic" or "neurotoxic" in the broadest way. It was only in view of the enhancing action of Freund's "adjuvants" generally in promoting antibody reactions that the experimental encephalomyelitis was assumed to have a similar antibody, and in consequence "allergic" mechanism. However, for the moment, we should note: (1) that the active agent in brain is apparently non-proteinous; (2) that no counterpart to the lesion is produced in other organs when other organs are used as sources of "antigen"; (3) that it is not possible to transfer the alleged sensitivity to brain in any way like that in which tuberculin sensitivity can be transferred passively; (4) that the histopathological lesions in the brain are not like those of other conditions more generally accepted as "allergic" in character; and (5) that anaphylactic and Arthus reactions can occur in treated animals independently of the encephalomyelitis. Finally, Lumsden *et al.* (1950) found that the antibody responses in the experimental animals, complex in pattern as they were in view of the complex antigenic nature of crude brain used as an inoculum, showed no evident parallelism or relationship with the encephalomyelitis.

Intrinsic Mechanism of Multiple Sclerosis

One possibly important factor is the highly specialized nature of myelin-sheath protoplasm with its uniquely high ratio of lipids to protein, a biochemical peculiarity shared perhaps only with the enveloping membrane of the erythrocyte. This latter analogy is indeed so close that the very active research being conducted just now on the biophysics of haemolysis may prove vital to our understanding also of the nature of demyelination. Exactly what the amounts of protein and lipoid are within the sheath is not yet known, but this would seem a problem now amenable to quantitative physical techniques like Caspersson's (1950) ultraviolet-light absorption and Engström's *x*-ray absorption methods (Engström and Lindström, 1950).

If the protein component of the sheath is so much less than in cytoplasm generally, and in the axoplasm in particular, it may reasonably be predicted that enzyme activity in the sheath will be correspondingly much less than in the axoplasm. Therefore, even though the sheath is structurally part of the nerve fibre it may reasonably be assumed that metabolic processes within the sheath are slower than in the axoplasm by a margin wide enough to permit the phenomenon of axomyelinic dissociation. This low "vitality" on the part of the sheath relative to the axon is indeed illustrated by its characteristic slowness to form *in vivo* as in Speidel's (1932a, 1932b, 1933) direct observations on the medullating nerves in the tadpole tail, and by recent observations on the development of myelin in tissue cultures of chick embryo dorsal root ganglion reported by Peterson (1950) from Murray's laboratory at Columbia University.

Possible Role of Enzymes

It might be said that by the tenets of modern biochemistry it is almost axiomatic that, whatever kills the myelin sheath, the final process of lipoid degradation will be mediated by enzymes. An examination of the structural formulae of sphingomyelin and of cerebroside, for instance, will give us a clue to the nature of some of the enzymes concerned in the hydrolysis of the more vulnerable linkages. We know, too, that the administration of such enzymes as the lecithinases of *Clostridium welchii* alpha-toxin and of cobra venom can lead to the splitting of crude myelin *in vitro* (Morrison and Zamecnik, 1950), and that *in vivo* the intracerebral injection of purified pancreatic lipase, for instance, can, according to Vogel (1950), cause pools of demyelination resembling plaques of multiple sclerosis. Then, again, there is reason to believe, as I have written elsewhere (Lumsden, 1950), that the brain can be induced by artificial means to liberate myelinolytic substances when certain as yet unidentified enzyme systems are poisoned by cyanides.

If we seek to understand how intrinsically produced myelinolytic ferments could cause multiple sclerosis, as Marburg postulated as long ago as 1906, our real problem is not to find possible sources of such ferments but to explain why in the ordinary processes of myelin degradation in diseases of the nervous system other than multiple sclerosis the action of these ferments is limited to those units already damaged directly by the causative noxa; in other words, why their action does not spread to the myelin of undamaged medullated axons.

In the past, attempts were made by Brickner (1930), Weil *et al.* (1935), Richards and Wolff (1940), and Weil and Heilbrunn (1941) to demonstrate myelinolytic substances in the blood, urine, and cerebrospinal fluid of patients with multiple sclerosis. The methods used, however, have not been sufficiently analytical nor have the results been generally accepted as quantitatively significant. The probability is that even if myelinolytic ferment is liberated within plaques it is utilized, neutralized, absorbed, or otherwise bound locally and does not enter the body fluids in measurable amounts. The logical necessity is therefore to devise a technique for measuring it *in situ*. I personally believe this should now be possible provided suitably fresh material can be

obtained immediately after death, or, preferably, by biopsy sample when for any reason surgical intervention has been undertaken.

To explore the possible application of the quantitative micro-methods of Linderström–Lang to this special type of problem, working in Glick's laboratory in Minneapolis, I have made a preliminary study of esterase activity in the sciatic nerve of the rabbit at varying intervals after transection. The details of the method and the results will be reported fully elsewhere. Twenty-micron frozen sections of the freshly removed nerves were incubated in micro-reaction tubes along with a suitable buffered substrate, methyl butyrate, and at suitable intervals the reaction was stopped by the addition of phenol and the *p*H change in the substrate determined by microtitration. Parallel runs were made with tissue without substrate, and others with substrate without tissue. The sections were taken at various levels above and below the line of transection and likewise in the corresponding levels of the contralateral (unsectioned) sciatic nerve. Esterase activity was in this way determined and finally expressed in terms of one milligram of dried tissue. Distal to transection, lipolytic activity falls immediately and progressively till a constant level is attained at about 40% of the normal activity of the normal whole nerve. This irreducible minimum we suspect measures the activity of the endoneurial and perineurial sheath cells, which, far from degenerating in the peripheral stump, undergo a proliferation exceeding in intensity that of the corresponding sheath cells in the central stump.

Meanwhile at the lower end of the portion of the nerve proximal to the transection there is, in the segment of regenerating neurites, a steady rise of lipolytic activity for about 30 days up to 300 to 400% of the normal. Then as reunion occurs the zone of highest activity passes into the upper extremity of the now reunited distal portion. With this method it is possible, too, to take sections adjacent to those used for microanalysis for ordinary fat and other histological stains, thus permitting qualitative histological and quantitative microchemical studies at the same time. In the same way, given suitable fresh material, it should be possible to make quantitative studies directly, at least of lipase activity to start with, in different regions of a multiple sclerosis plaque.

Conclusion

Until the hypothesis that there is produced within plaques a myelinolytic ferment which diffuses slowly into the surrounding white matter is confirmed or refuted in this way it is perhaps premature to speculate too far upon the possible mechanism of its production. However, when we take account of what is now known chemically of the close relationship, if not identity, of genes and enzymes, and of the role of vitamins and hormones as prosthetic components of enzymes, a whole world of light is shed upon our present problems. In the leucodystrophies and in the myelin lesions of the general lipoidoses it may be postulated that the missing enzyme is a gene. In the system demyelinations like subacute combined degeneration of the cord and "swayback" it is probably a deficiency of some prosthetic group. For instance, in subacute combined degeneration it is almost certainly due to a deficiency of the cobalt-containing *crystalline red substance* isolated by Lester Smith (1948) in this country.

In the case of "swayback" the deficient factor is apparently connected with copper, though copper parenterally in inorganic or organic form is useless. It is probable, then, that the copper must be bound in a specific complex before it is presented to the neural tissue and that it forms part of an essential prosthetic group, as for instance does zinc in carbonic anhydrase. But we do not know what precisely is the role of the trace-element copper apart from the fact that it is essential for the formation and maintenance of the enzymes cytochrome oxidase and catalase.

It would seem, then, that insufficiency of essential enzymes would be enough to explain the genetically determined and the nutritional deficiency forms of myelin dyscrasia. But in addition to containing enzymes necessary for the synthesis and maintenance of myelin it seems fairly evident from the experiment I have described on esterase activity in Wallerian degeneration that the *normal* nerve fibre, apparently independently of extrinsic cells, contains the enzymes necessary for myelin catabolism. In other words, the living medullated nerve fibre contains not only myelin lipoids but the specific enzymes which hydrolyse them. One is reminded that this is no remarkable paradox by the classical analogy of Claude Bernard's that the liver cell contains both glycogen and diastase.

In the same way acetylcholine, cholinesterase, and choline acetylase all exist together at the nerve ending, and probably also, as Nachmansohn (1946) has shown, along the whole surface length of the nerve. And again, prothrombin, thrombokinase, and calcium can exist together without clotting, as a result, we say, of the presence here also of a specific antagonistic ferment. In the same way we may postulate that myelin contains not only phospholipases and cerebrosidases but also antiphospholipases and anticerebrosidases. Since on theoretical physical chemical grounds it is thought highly probable that hydrolysing enzymes act at the cell boundary, we may envisage the antiferment molecules arranged as a monomolecular layer immediately outside the lipolytic ferment layers.

Can we then postulate, too, a direct connexion between this layer of antiferment molecules and the peculiar morphology of the oligodendrocyte with its highly tenuous and fragile protoplasm arranged, as the exquisite illustrations of del Rio Hortega have shown us, like a delicate bandage-like membrane just outside the myelin sheath? To destroy selectively the oligodendrocyte and yet to leave a living myelinated axon would then permit the hydrolysing ferment to destroy the myelin. This in turn would permit the diffusion from the *still living axoplasm* of lipolytic ferment, which in turn would damage the oligodendrocytes in the next rank of these cells, so setting in process a chain reaction of myelin disintegration diffusing out slowly like an oil-stain through the white matter.

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ASPHYXIA NEONATORUM TREATED BY ELECTRICAL STIMULATION OF THE PHRENIC NERVE

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Sarnoff and his colleagues (1948, 1950) have recently reintroduced an old method of artificial respiration by the electrical stimulation of the phrenic nerve in the neck through the intact skin. This method was first used as far back as 1783 by Hufeland, who discharged a series of condensers through the patient. The method was again tried after the discovery of electromagnetic induction, when the shocking coil was used. Israel (1927, 1928) reported the use of the shocking coil for the resuscitation of newborn infants, and was most impressed with the results obtained. With modern equipment it is possible to obtain a controlled and smoother contraction of the diaphragm than was previously possible.

Description of Apparatus

The electrical wave-form used to stimulate respiratory movements when applied to the phrenic nerve consists of negative-going rectangular pulses of ½ millisecond

duration repeated at intervals of approximately 10 milliseconds. The pulses increase linearly in amplitude until they reach a maximum, when, after a further short period of stimulation, they cease. This complete cycle is repeated at a rate of 18 times a minute, the period of stimulation occupying two-thirds of the cycle and a rest period occupying the other one-third.

In our instrument all these qualities were made variable, but the values given here are those we have found most suitable in practice, and in any commercial instruments these could be pre-set. The output intensity can be controlled and, as can be seen from the diagram, currents as large as 110 mA peak were found necessary.

The apparatus is similar to that used in electrotherapy. It consists of a double triode valve connected as a multivibrator feeding the screen grid of a pentode output valve via a cathode follower. The control grid is fed with negative-going saw-tooth waves from a squegging oscillator. The output is obtained from the anode of the pentode via a large condenser, thus making the mean current zero and avoiding polarization within the tissues. The power for the apparatus is supplied from the 230 v. A.C. supply.

Technique of Treatment

The active electrode is a silver-plated probe, the end of which is covered with a single layer of lint soaked in saturated saline immediately before use. This electrode makes contact with an oval area of about 8 by 6 mm. on the baby's neck. The infant is placed supine, lying on the rectangular indifferent electrode (made of electrode metal), 14 by 5 cm. in area. This electrode is also covered by lint soaked in saline.

The position of the most readily accessible part of the phrenic nerve was carefully described by Duchenne de Boulogne in 1851, and is above Erb's point. With the head turned to the opposite side the phrenic nerve is found just behind the sternomastoid muscle at the junction of the middle and lower thirds of that muscle. With use of the electrodes described, muscles other than the ipsilateral diaphragm are often stimulated, and most commonly the arm was abducted from the side with each stimulation. We have not sought to confine stimulation to the phrenic nerve alone by using a smaller electrode, because this arm movement will assist expansion of the lungs. When the phrenic nerve is being stimulated the epigastrium is seen to protrude chiefly on the side being treated.

Additional evidence of diaphragmatic movement is obtained by hearing the inspiration, with or without the stethoscope, and when the Rotunda oxygen mask (referred to below) was being used one could on occasion see the rubber reservoir diminish in size. More effective inspirations can be caused by the bilateral stimulation of both phrenic nerves; this was attempted in a few cases, but it is more difficult for a single operator to apply and to maintain the electrodes in the correct position. When only one active electrode was being used it was our practice, in cases which required prolonged treatment, to change from time to time the side of stimulation.

A peak current of 3–5 mA through the electrodes described is sufficient to provide adequate ventilation in the adult. When we tried to resuscitate babies we soon realized that larger currents were necessary. For this reason, and in order to obtain quantitative data, a second stimulator was constructed which contained a peak-reading voltmeter consisting of a calibrated cathode-ray tube and an ohmmeter. When the right instrument was available—for both were in use—and there was time to make observations, readings of potential difference and resistance were noted when "adequate movement of the diaphragm" occurred. From these two readings the peak current was calculated, but this figure can be regarded only as an approximation, as the current wave-form will not be identical with the voltage wave-form; also the resistance between the electrodes may not be the same when pulses are applied as when a direct current meter reading is taken.

Experimental Investigation

The present investigation was undertaken in two parts. From May, 1949, until July, 1950, we had the instrument available in the home of one of us and made arrangements to be called to St. Mary's Hospital, the Postgraduate Medical School, and Queen Charlotte's Hospital when cases of foetal distress or neonatal asphyxia arose. In this phase of the investigation we had only two successful cases; in the 30 other calls we received the baby had either recovered or died by the time we arrived. The useful control period caused by the delay in arriving at the hospital was clearly too long for all but the exceptional cases. For a period of nine weeks, from July to September, 1950, one of us (K.W.C.), financed by a grant from the Medical Research Council, was enabled to work in the Rotunda and the Coombe Hospitals in Dublin. During this period there were 1,083 deliveries of viable foetuses in the labour wards of the two hospitals, and on most occasions it was possible to be present within 10 minutes of a call.

As the cases reported here have been delivered at five different hospitals, and this treatment was applied only at the invitation of the responsible clinicians, there was a widely varying background of other methods of resuscitation which was not under our control. Before attempting to stimulate the phrenic nerve we insisted only that the air passages of the baby should be emptied as thoroughly as possible, by mucus catheter or by direct intubation, depending on the practice of the hospital. While stimulation was proceeding oxygen was applied, again by one of several methods, but the best and simplest seemed to be a baby-sized anaesthetic mask and balloon reservoir which was in use at the Rotunda Hospital. Even with the excellent co-operation which we received in Dublin it was neither possible to be present with the stimulator at every delivery nor possible to be called to every second asphyxiated case. We can report, therefore, only the results we obtained, and it will not be possible to deduce from this investigation whether neonatal morbidity or mortality would be affected in a statistically significant fashion by this method of treatment.

Before a baby was treated an assessment was made of its clinical condition. We have used the simple classification of "slightly," "moderately," and "severely" ill infants, but we would stress that this diagnosis had to be made rapidly and the gradations are not clearly defined. "Slightly ill" babies were those who at birth had moderate but diminished muscular tone and were somewhat cyanosed. They would generally have taken some spontaneous respirations but had not established adequate oxygenation as judged by the colour of the mucous membranes. "Moderately ill" babies were those who appeared to have no muscular tone and were very deeply cyanosed.

"Severely ill" babies had no muscular tone, generally had taken no respirations at all, had relaxation of the anal sphincter, and included those who had white asphyxia. All babies treated in Dublin were followed to their own homes after discharge, and an attempt was made to get the mothers to bring them back to their hospitals. Dr. W. D. Brophy has kindly seen those at the Rotunda.

The results of our investigation are divided into four sections. Each section is completed by the inclusion of the appropriate case histories. The total number of cases treated was 29, of which 25 recovered. Measurements were made on 19 of the cases.

(a) Relation between Current and Degree of Illness

The diagram shows the current required, as defined above, in those babies in whom measurements were made. In some cases it was possible to make more than one measurement, and the clinical conditions of the infant might have altered in the interval. The points joined by a line indicate repeated observations on one infant and the arrow indicates the passage of time.

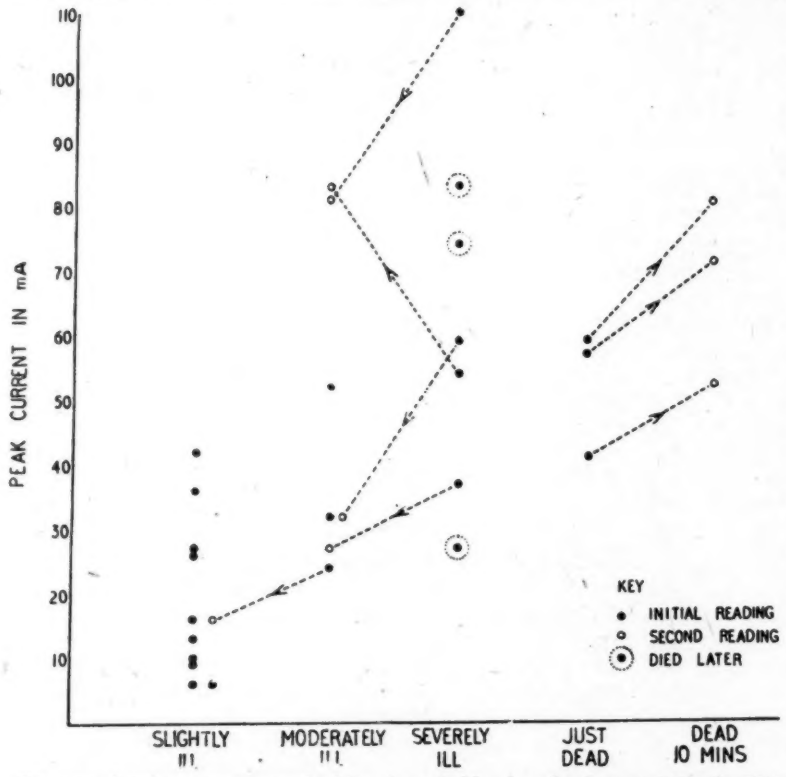

Diagram showing currents required for those babies in whom measurements were made.

It will be observed that there seems to be some relationship between the current required and the sickness of the baby, as defined above. We feel that this relationship is a function of the neuromuscular system under consideration and not other factors, for the following reasons: (1) When, after a period of stimulation, the neck at the site of the electrode and the skin of the back underlying the indifferent electrode were thoroughly cleaned with ether the resistance diminished slightly but the current required was not lowered. (2) If more than one reading was possible on a baby the current required diminished (in all but one case) if the baby was improving and increased the longer the baby was dead, and there were not necessarily parallel skin-resistance changes.

If it is correct to say that the current required for stimulation is a function of the sickness of the baby, this is most probably related to the degree of oxygenation of the tissues, which can be correlated with *in vitro* observations on muscle-nerve preparations. These show that in anoxia a stronger stimulus is required to evoke a maximal response of nerve (Lorente de Nó, 1947).

(b) Expansion of the Lungs by Phrenic-nerve Stimulation Alone

In most of the cases in which death subsequently occurred the baby had taken some spontaneous respirations before death, but we have pathological material from three cases in which the time of death was accurately known and the baby had taken no respirations and no other method of artificial respiration had been used. This material gives us information whether stimulation of the phrenic nerve alone, with adequate movement of the diaphragm, is capable of expanding the lungs. This is important, for more effort is necessary to separate the adherent alveolar surfaces than to take subsequent breaths (Wilson and Farber, 1933).

Case Histories

Case 1. St. Mary's Hospital.—The patient was born on April 5, 1950, and was a second female twin born 75 minutes after the first. At delivery the child was blue and flaccid and made no attempt to breathe. The heart was slow and stopped 13 minutes later. Stimulation was started on the right phrenic nerve two minutes after the heart had stopped. Dr. J. P. M. Tizard auscultated the chest while this proceeded; he heard an air-entry over the right lower chest anteriorly and noted that the heart restarted at 16 beats a minute. Stimulation rapidly became less effective and the heart stopped. After five minutes the stimulation was quite ineffective and was not continued. Post-mortem examination showed that there was almost complete aeration of the right middle lobe and some aeration of the right lower lobe. The heart showed a bicuspid aortic valve and the brain bilateral superficial tentorial tears.

Case 2. Coombe Hospital.—This patient was born on July 30, 1950, by breech delivery. The foetal heart was irregular and rapid. The after-coming head very suddenly passed through the pelvis and delivery occurred five minutes later. The heart beat could not be heard or felt and there were no signs of life. Phrenic-nerve stimulation was applied first on the right side and then on the left, with more effect on the right. Post-mortem examination 24 hours later showed that the whole thoracic pluck sank in water, but the right lung by itself floated, while the left sank. There were bilateral tentorial tears. Section showed moderate aeration of the right lung.

Case 3. Rotunda Hospital.—This was a case of difficult forceps delivery on August 8, 1950. The heart rate at delivery was 60 a minute, but this stopped in five minutes. There were no respiratory movements. Stimulation started directly after the heart had stopped, with reasonably effective movement of the diaphragm; the left side was stimulated more than the right. Post-mortem examination 12 hours later showed bilateral tentorial tears, right greater than left.

The entire thoracic pluck floated. Sections showed moderate aeration but many intra-alveolar squames.

From these cases we conclude that this method of artificial respiration is capable of expanding the lungs, in which respect it does not differ from other techniques, but here the normal muscles are being called into play and there cannot be the danger of pulmonary emphysema or distension of the stomach, which are present with the positive-pressure methods.

(c) Evidence for the Efficacy of the Method in Saving Life

From the Table it is seen that four babies died out of the 29 treated. Of the 25 who lived all of those slightly ill and moderately ill survived (except the one case discussed below). As the chance of survival without aid is greatest for those least ill it is obvious that the efficacy of the method would be best illustrated by those cases which were severely ill. However, bearing in mind our definition of degrees of illness, we believe that the figures for those less than severely ill show promise for the method. The four cases in which the patients were thought to be severely ill and subsequently died are here described.

Results of Cases Treated

Condition	No.	Recovered	Died	Average Current (Initial Reading) (mA)	No. of Observations of Initial Reading
Slightly ill ..	14	14*	0*	20	9
Moderately ill	6	6	0	36	3
Severely ill ..	9	5	4	61	7

* One died at 13 weeks and 1 day (see text).

Four Fatal Cases

Case 4. Rotunda Hospital.—The mother was a primipara and was admitted, one week post-mature with a floating head, for induction of labour. Castor oil, a hot bath, and an enema were given, and also quinine and "pitocin." The membranes ruptured spontaneously on July 13, 1950, labour began on the 15th, and meconium was noticed in the early hours of the 16th. At midday a vaginal examination revealed that the os was still only three-quarters dilated and the occiput was posterior in the high mid-strait. There was a large caput and the head appeared to be jammed in the pelvis. The anaesthetic was continued and the patient taken to the theatre for caesarean section. The head was difficult to disengage from the pelvis, and there was a great deal of meconium in the amniotic fluid.

A male infant of 8 lb. (3.6 kg.) was delivered at 12.35 p.m. He was completely flaccid and the heart was beating slowly. Phrenic-nerve stimulation was attempted after pharyngeal aspiration, but, although the abdomen moved, the effect was poor and an air entry could not be heard. Oxygen was given by mask. The baby gradually became pink and cried a little. He was put in an oxygen tent and large quantities of fluid and meconium continued to come from the mouth and nose. When he became more blue direct intubation was attempted and oxygen was run in by catheter. He died at 4.30 p.m.

Post-mortem examination showed that there was a large left-sided pneumothorax, with a collapsed left lung and one emphysematous bulla on the lingula. The right lung was also collapsed. There were some clots over the posterior hemispheres of the brain. It seems almost certain that the pneumothorax was the result of the positive-pressure oxygen therapy which was given without an adequate safety valve.

Case 5. Coombe Hospital.—This baby was the second of twins and was born on August 18, 1950, with the cord round the neck; delivery was by breech extraction after some placental separation. The heart had been slow before delivery and stopped after delivery. It had started again with an intracardiac injection of nikethamide, and mouth-to-mouth respiration was used. Phrenic-nerve stimulation was started 25 minutes after delivery and good breath sounds were heard with each stimulation. Treatment was stopped after 20 minutes, and the baby remained pink in an oxygen tent. The infant died 24 hours after birth, shortly after being given a feed from a teaspoon while lying in the tent. Post-mortem examination showed that the lungs were moderately well aerated. There was evidence of inhalation of amniotic debris and signs of early bronchopneumonia. Small bilateral tentorial tears were present, with very little haemorrhage.

Case 6. Rotunda Hospital.—The baby was born on August 21, 1950, and weighed 5 lb. 10 oz. (2.6 kg.). It was delivered by an emergency lower-segment caesarean section for severe ante-partum haemorrhage with air hunger. At birth the baby had white asphyxia without response to skin stimulation. A good colour was rapidly obtained with phrenic-nerve stimulation. Two days after birth the baby's condition was not satisfactory. *X*-ray examination did not reveal any massive collapse of the lungs. Death occurred three days after birth. At post-mortem examination there were some subarachnoid haemorrhages over the posterior part of the frontal lobes and some extravasation of blood in the right tentorium. The right lung floated in water, but the left sank.

Case 7.—Rotunda Hospital.—This was a case of difficult forceps delivery on August 3, 1950; the baby was blue and flaccid. It was treated with moderate success 20 minutes after delivery, and breathed spontaneously and irregularly after half an hour's treatment. It was kept in an oxygen tent, but respiration improved only slightly, and it brought up large quantities of blood-stained mucus. Death occurred 12 hours after delivery. Post-mortem examination showed bilateral blood-stained pleural effusions and apparent haemorrhages in the lungs. The upper lobes floated in water, the lower lobes sank. There was some extravasation of blood around the right suprarenal gland. The brain was normal. Sections showed emboli in the pulmonary arteries, a finding with which we were previously unfamiliar.

Severely Ill Patients Who Survived

The following five reports are of patients who were thought to be severely ill and who have lived.

Case 8. St. Mary's Hospital.—This case has been previously described (Cross, 1950). The patient was under Dr. Reginald Lightwood and Mr. Leslie Williams. Briefly, after a difficult instrumental delivery per vaginam, there was a period of three and a quarter hours' severe cyanosis with irregular gasping respiration. The baby was twice thought to be dead by the resident obstetric officer, and immediately before treatment was started single gasps were being made at less than one a minute. Three-quarters of an hour's treatment with the stimulator rendered the baby pink and capable of adequate spontaneous respiration. This baby has been followed up by Dr. Lightwood for 20 months; he reports that the baby milestones have been passed at normal times and that this infant appears to be in all respects normal.

Case 9. Rotunda Hospital.—Lower-segment caesarean section was performed on August 5, 1950, for prolapse of the arm and cord of 1 hour and 40 minutes' duration with marginal placenta praevia. An 8-lb. (3.6-kg.) baby was delivered with marked asphyxia pallida; it made no attempt at spontaneous respiration. There was an immediate and excellent response to phrenic-nerve stimulation, which was discontinued within three minutes, as the baby was then pink and breathing satisfactorily. It has made excellent progress, weighing 13 lb. 12 oz. (6.2 kg.) at 12 weeks.

Case 10. Rotunda Hospital.—This baby—6 lb. 11 oz. (3 kg.)—was born on August 16, 1950, after a very difficult forceps delivery, when the mother had been 64 hours in labour. After bathing in hot and cold water and being given oxygen for 10 minutes from the Rotunda mask,

phrenic-nerve stimulation was continued for 15 minutes with only moderately good air entry, and the baby was then left in an oxygen tent breathing spontaneously. Since discharge the baby has made very good progress and is developing normally. Weight 12 lb. 2 oz. (5.5 kg.) at 12 weeks.

Case 11. Rotunda Hospital.—The mother suffered from toxaemia of pregnancy, and forceps delivery was undertaken for transverse arrest of the head. At birth—weight 8 lb. 2 oz. (3.7 kg.)—the face of the baby was blue, but the body was strikingly white and flaccid. After bathing in hot water and skin stimulation had failed, satisfactory stimulation of the phrenic nerve was carried out for 10 minutes, at the end of which time spontaneous respirations were occurring often enough to keep the baby pink in an oxygen tent. Progress since discharge has been good, the weight at 12 weeks being 13 lb. 12 oz. (6.2 kg.).

Case 12. Rotunda Hospital.—A multipara was delivered on July 24, 1950, of an 8-lb. (3.6-kg.) female child by breech extraction. The right arm had been extended and the left was in the nuchal position. Twenty minutes after delivery the baby was flaccid and blue, and had taken no spontaneous respiration. Positive-pressure artificial respiration had been given from the Rotunda oxygen mask with little or no improvement. Good response to phrenic-nerve stimulation was obtained, and after 10 minutes' treatment the baby was breathing spontaneously. She had gained 8 oz. (227 g.) by the seventh day, when mother and child were discharged from the hospital. The home is rather poor, but the baby was progressing satisfactorily at 8 weeks, when she weighed 10 lb. 11 oz. (4.8 kg.) The mother has not responded to repeated appeals to bring the baby for examination.

An examination of these results cannot give certain evidence of the efficacy of the method, but in the opinion of the clinicians responsible and the labour ward sisters all those labelled severely ill were thought to be dying, yet five of the nine have lived. In the four cases in which death occurred it appears that causes other than neonatal asphyxia could be put forward.

(d) After-effects of Electrical Stimulation

As the current we were using was considerably larger than that required for the adult, we thought it was necessary to examine those babies who recovered to see if there was any sign of permanent injury from the high dosage which had been employed. All but two of the babies who have survived the neonatal period have been followed up for three months and no damage has been noted, although we must confess that the examination was a rather general one, for there was no specific type of injury which we could visualize as being likely to arise.

One patient, the first of twins, who had been regarded as slightly ill at birth, died at the age of 13 weeks. Forceps were applied for persistent occipito-posterior position, and on delivery the baby was breathing poorly and was somewhat cyanosed. Good respiratory movements were obtained with a peak current of only 11 mA. After discharge both twins had made slow progress, which was not surprising, as it was with some difficulty that the mother was persuaded to increase the diet above 3 oz. (85 ml.) of half milk and water with four teaspoonfuls of sugar only three times a day. At 12 weeks of age the baby weighed 8 lb. 11 oz. (3.9 kg.), which represented a gain of 9 oz. (255 g.) less than her sister in the same period, and was well below the average rate of gain for the group. The child was unexpectedly found dead, and post-mortem examination showed severe congestion of both lungs, with many alveoli filled with exudate; these changes were consistent with pneumonia.

It is still too early to say whether the resuscitation of babies who had suffered from severe cyanosis has resulted in children with any mental derangement. Case 8, however, has so far showed no signs of abnormality.

We have failed to find any ill effects attributable to phrenic-nerve stimulation or any other abnormalities which may result from the survival of a severely cyanosed child.

Discussion

Whenever measurements are made it is necessary to give some idea of the errors involved. In Section (a) above, errors in the potential and resistance readings, together with other undetermined instrumental errors, probably amount to 10%, but there are two large errors which we have not estimated: (1) The current necessary to obtain "adequate movement of the diaphragm" will depend very greatly on the positioning of the electrodes, and this will vary from case to case and also during any one case; (2) the process of estimating when "adequate movement of the diaphragm" is obtained is itself subject to a large error, for diaphragmatic movement is estimated from the protrusion of the abdomen. Both these errors are unsatisfactory, but under the urgent conditions of treating these babies, many of whom seemed moribund, we did not consider it necessary at this stage to improve our methods.

The exact choice of ¼ millisecond pulse duration is not entirely arbitrary. It is long enough to induce a propagated response in the nerve, but is probably too short to excite muscles directly in the adult with the current used for operation. This factor is useful in experimental work with the adult. It appeared, however, that we generally caused direct stimulation of the sternomastoid in the infant, quite apart from other muscles supplied by the upper part of the brachial plexus; we have not sought to avoid this, because the movement produced would tend only to expand the thorax, and this effect can be increased by fixing the arm in an abducted position. This was well shown in one baby, not mentioned in this series because he had multiple congenital abnormalities, including a grossly deficient diaphragm. By stimulating the accessory muscles we improved the colour of the infant and air entry was heard, although there was never any visible movement of the epigastrium.

The effects of phrenic-nerve stimulation in the newborn seem to differ markedly from those in the adult, in that inhibition of spontaneous respiration, which is reported by Sarnoff and which we confirmed in the adult, does not occur. This has the advantage that the dangers of overventilation are not so great as we had at first feared. Stimulation is stopped when the baby is no longer cyanosed, and is restarted if cyanosis returns.

The repetition frequency of stimulation of 100 c./sec. is high enough to ensure a smooth contraction of the diaphragm and has the advantage that it can be locked to the mains supply frequency.

We would suggest that those who intend to use the apparatus can best familiarize themselves with the anatomy of the part by experimenting on their own phrenic nerves. For self-experimentation, and when one is working on an infant, it is convenient to have the machine fitted with a loudspeaker so that a buzz is made when impulses are passing and one can correlate the noise with any movement the infant may make.

It is clearly not possible to compare our results with those obtained with other methods, for the series is too small and too many factors enter into the consideration

of each case. Such a comparison is urgently required and should be undertaken in centres where there is an established routine for treating neonatal asphyxia, and where enough cases of this variable condition occur, so that treated cases and controls can be studied.

Summary

An instrument is described which is capable of performing artificial resuscitation when electrodes are applied to the neck over the site of the phrenic nerve. Experiments on the treatment of asphyxia neonatorum are described together with appropriate case histories taken from 29 subjects. Results are given which show the method to be promising and the line for further experiments is suggested.

This work has been possible only because of the kind co-operation of many people, as our appointments carry no clinical responsibilities. Post-mortem examinations of most of the cases at the Rotunda Hospital were made by Dr. J. H. D. Widdes and the pathological material was examined by Professor W. D. Newcomb and Dr. D. M. Pryce, to all of whom we are very grateful. We would also like to thank the Medical Committees of the English hospitals, the Masters and staff of the Rotunda and Coombe Hospitals, and the many clinicians who have co-operated with us. Our thanks are particularly due to the Medical Research Council for a grant to one of us (K. W. C.) which made possible the clinical work at Dublin, and to Mr. K. F. Tindall for help in constructing the instruments.

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The pioneer health centre of the Union of South Africa was set up at Polela, Natal, in 1940, and up to date 39 have been opened. They aim primarily to prevent disease and to promote health, but curative medical treatment is also given. On the whole patients are encouraged to go to private practitioners in case of illness, so no encroachment is made on private practice; on the contrary, routine medical examinations and home visits result in more patients attending the doctors' surgeries. All persons in the area covered by a centre, whether they are ill or not, are encouraged to attend the centre for routine medical examination, and the assessment of health and ill-health is based on environmental and social as well as individual pathology. Preventive services such as immunization against infectious diseases, antenatal examinations, and so on are provided by the centres. Each centre is left as much freedom as possible to carry out experiments and adapt itself to local needs; in short, each is a research centre. They are still embryonic; the training scheme being developed in Durban plans to give each medical officer a minimum of six months' training, and to appoint at least two to every centre, preferably one man and one woman. The health-centre movement has had to cope with both official prejudices and the opposition of herbalists and witch-doctors. One of their biggest advantages is the scope they give for the employment of the African on health work among his own people. They cater mainly for Africans, but also for non-Europeans and in certain cases Europeans; one result of their work is the increasing confidence the people are showing in hospital treatment (see *S. Afr. med. J.*, 1946, **20**, 326). The centres are also educating in sanitation, diet, and hygiene.

BRUCELLA ABORTUS ENDOCARDITIS

BY

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Infections due to *Brucella abortus* are not uncommon in this country. They remain long undiagnosed and for many months blood-stream infection persists. Until recently, no therapy was effective. It is therefore surprising that no fully proved case of endocarditis due to this organism has so far been recorded in British journals, although in 1936 Rennie and Young described a case which was not proved bacteriologically at necropsy. To date, only three reported cases can be said to satisfy all the required criteria in life and at necropsy (Rothman, 1935; Spink and Nelson, 1939; Spink, Titrud, and Kabler, 1942).

Chemotherapy and antibiotics have yet to be proved effectual in Brucella endocarditis. Spink *et al.* (1948) reported a case in which streptomycin and sulphadiazine appear to have inhibited the growing powers of the organism but did not save the patient.

Now that aureomycin and chloramphenicol have both been given with satisfactory results in uncomplicated *Br. abortus* infections, the following case is worth reporting, as courses of "aureomycin," chloramphenicol, penicillin, and streptomycin did nothing to alter the progress of the disease. Admittedly chloramphenicol was given too late to have any effect, but with none of the drugs mentioned was the fever lowered; in fact a Jarisch–Herxheimer reaction appeared to be caused by aureomycin. Dihydrostreptomycin together with aureomycin as used by Heilman (1949) and Herrell and Barber (1949) was contemplated, but was withheld until too late.

Case History

The patient, a male labourer aged 48, was first noticed to have a "bad heart" at the age of 7. In 1917 he was rejected for military service on this account. As he had suffered from dyspepsia for the past five years he had been drawing extra unpasteurized milk from the estate on which he worked in order to supplement his gastric diet.

He was first seen in the out-patient department on July 26, 1949, complaining of palpitations of six months' duration, malaise and fatigue for one year, and shivering attacks with night sweats for three weeks. The heart was found clinically to be enlarged to the left. Loud harsh systolic and faint soft diastolic murmurs were heard at the aortic area, and a systolic thrill was palpable at the same site. The E.C.G. was normal; haemoglobin 92% (Haldane); screening and radiographs of the heart showed some prominence of the ascending aorta, rounding of the cardiac apex with slight enlargement of the left ventricle, and calcification of the aortic valves. Clinically and radiologically the picture was that of aortic stenosis, compatible with the diagnosis of a long-standing rheumatic condition.

He returned on August 17, 1949, with fever, and was admitted as a case of subacute bacterial endocarditis superimposed on a long-standing rheumatic aortic stenosis. His temperature was ranging between 100 and 104° F. (37.8 and 40° C.). His B.P. was 120/85. Slight clubbing of the

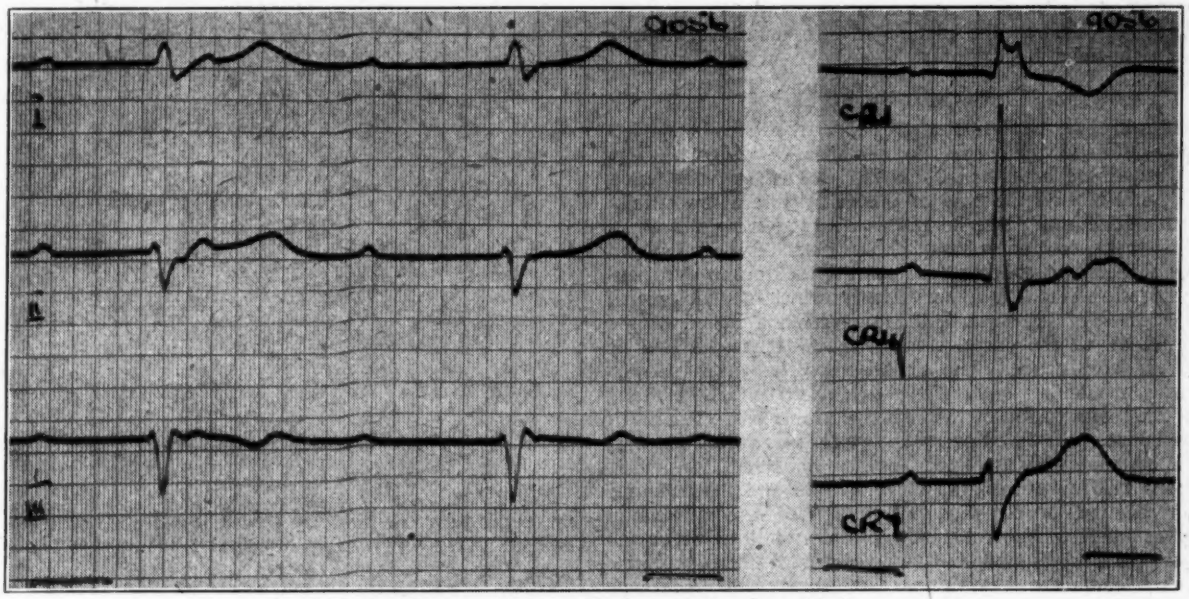

FIG. 1.—Electrocardiogram showing complete heart-block.

fingers was present. Three successive blood cultures yielded a pure growth of *Br. abortus*, and the serum agglutinated the organism to a titre of 1/5,000.

In spite of his high fever he did not complain, and he looked far from being a very sick man. He was treated with penicillin, 2,000,000 units daily, for 11 days without improvement.

On August 30 aureomycin was started, 500 mg. by mouth, four times daily. On this drug the temperature, pulse, and respiration rates became higher and more swinging in type, and after 48 hours' treatment the patient complained of acute pain in the left side of the abdomen and left testis. These symptoms developed rapidly in a symptom-free patient and disappeared a few days later. After 14 days the dose of aureomycin was increased to 750 mg. four times a day, and two days later to 1 g. four times a day. The drug was stopped on September 23 after 25 days' administration (total, 60 g.) without apparent effect.

Streptomycin was given from October 10 to 18, 1 g. daily (total 8.5 g.), without appreciable effect. On October 28 penicillin, 250,000 units twice daily, was given for boils in the neck, pus from which yielded a pure growth of *Staph: pyogenes*. Under treatment the boils rapidly subsided. About this time the fever abated and he was allowed up.

Throughout his stay in hospital the patient had felt well and his physical signs had remained virtually unchanged. At no time was the spleen palpable, and only on admission were a few doubtful petechiae noted. He was transferred to the hospital convalescent home on November 11, still slightly febrile—temperature 98–100° F. (36.7–37.8° C.). Blood culture had been negative since August 30, and, judging by his temperature-pulse-respiration chart, he had apparently made a slow and gradual improvement during his three months in hospital.

At the third week of his convalescence he began to feel ill, his temperature rose to 102.5° F. (39.15° C.), and he developed severe pains in his joints, especially his knees and the interphalangeal joints of his hands. His pulse rate lay between 60 and 85. On December 1, the day before he returned to hospital, he experienced his first "blackout," which consisted of a peculiar faint sensation without loss of consciousness. Subsequently these sensations occurred two or three times a day. No physical signs were found during such bouts, and his pulse remained regular.

On December 2 he re-entered hospital, a sick-looking, pale, sallow man—an entirely different picture from that of three weeks previously. The soft diastolic murmur at the aortic area was now marked. His pulse became slow the day after admission, rose subsequently to normal, and then dropped to 50, with a pyrexia of 99–102° F. (37.2–38.9° C.). Auricular sounds could be heard occurring in diastole, and a diagnosis of complete heart-block was made; this was confirmed by E.C.G. (Fig. 1), which showed also a right bundle-branch block. Two days later a second E.C.G. showed a complete A–V block persisting. Most of the ventricular complexes were now normal; only a single short run showed right bundle-branch block.

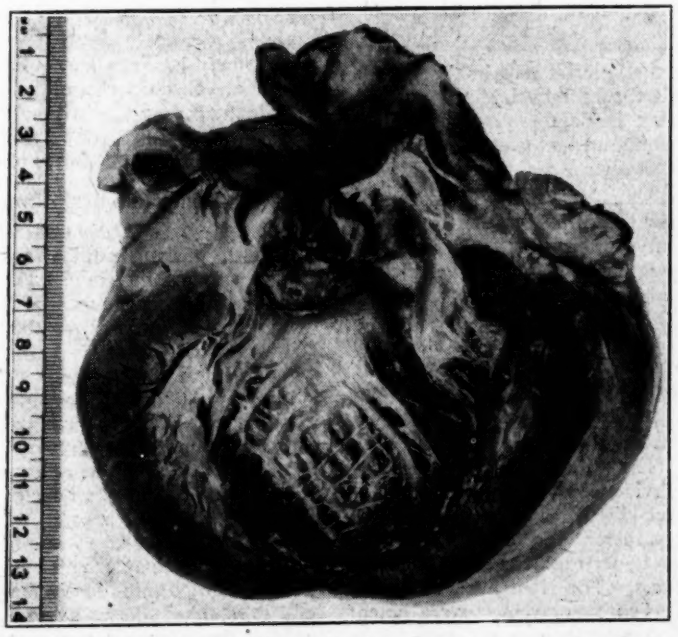

FIG. 2.—Photograph of heart showing vegetations on aortic valve.

Chloramphenicol therapy was started, 250 mg. two-hourly, on December 7, but two days later nocturnal coughing and dyspnoea rapidly developed, with considerable restlessness and great apprehension. Oxygen afforded some relief. Further attacks occurred, and at 4.40 p.m. on December 9, almost five months after his first attendance, he died with marked pulmonary oedema. His pulse rate before death was 40–50 a minute.

Radiographs taken with a portable apparatus on the last day of life showed the picture of left ventricular failure with right-sided hydrothorax.

Necropsy Report

At necropsy, 64 hours after death, the body was well nourished, and there was no evidence of oedema. The pericardial sac contained 3 oz. (85 ml.) of straw-coloured fluid, and around the base of the heart were a few stringy fibrous adhesions. The heart was enlarged (525 g.), mainly owing to hypertrophy of the left ventricle. The aortic valve showed bacterial endocarditis superimposed on an old rheumatic lesion (Fig. 2). The valvular orifice was obstructed by a mass of vegetations, 25 mm. thick, attached to the margin of all the cusps, creamy yellow in colour and of rubbery consistence. The underlying valve cusps showed fibrous thickening and calcification, both clearly of long standing, with fusion of the two posterior cusps. The partition between the fused cusps had undergone recent perforation, so that only its upper border remained, forming a fibrous bridge between the valve margin and the posterior wall of the aorta, thus allowing free communication between the respective sinuses of Valsalva, into which the ulcerative process had extended. Each of these posterior sinuses contained vegetations, and each had undergone distinct aneurysmal dilatation. That on the left had caused a bulging into the medial wall of the left auricle (Fig. 3),

FIG. 3.—Photograph of heart showing left auricle laid open to expose a swelling in the anterior part of the interauricular septum.

25 mm. broad, and involving the anterior part of the auricular septum. On incising this, haemorrhagic fluid escaped from a chronic abscess, 8 mm. in depth, lying just below the septal endocardium and communicating deeply with the vegetations in the sinus of Valsalva.

The aneurysm of the right sinus of Valsalva had caused a similar bulging into the right ventricle in the region of the infundibulum. The infective process in its recesses had also spread through the upper part of the interventricular septum to involve the medial cusp of the tricuspid valve, which was tacked down to the septum at this point. Ulceration had spread through the substance of the cusp, and from its free margin a polypoid vegetation, 3 cm. long and 1 cm. broad at its bulbous tip, was projecting into the right ventricular cavity (Fig. 4).

The left ventricle was dilated and hypertrophied, its average thickness being 18 mm. The mitral valve ring admitted three fingers, but showed no evidence of old or recent endocarditis. The left auricle was dilated, and in its auricular appendage was a small pale adherent thrombus. The right ventricle was dilated but not hypertrophied. The tricuspid valve ring admitted five fingers. The right auricle showed terminal dilatation only. The coronary vessels were patent throughout.

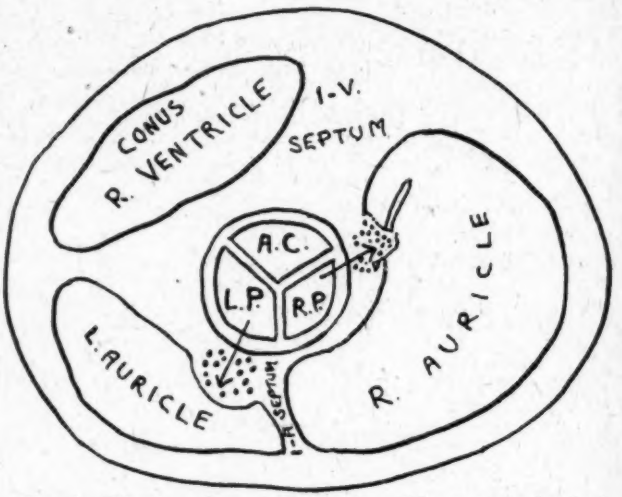

FIG. 4.—Diagram of transverse section of heart at the level of the aortic valve, to show the spread of infection to the interauricular septum and to the medial cusp of the tricuspid valve.

There were moderate passive congestion of the lungs, subacute congestion of the liver, enlargement of the spleen (227 g.), which contained a yellow resolving infarct, and a healed infarct in the right kidney. In other respects the kidneys looked normal.

Microscopical Examination

Heart.—The aortic vegetations were composed of dense masses of fibrin containing numerous clumps, morphologically Brucella. The aortic cusps were thickened by old hyaline fibrosis, with some calcification. The haemorrhagic abscess bulging into the left auricle had a wall composed of necrotic myocardial fibres, infiltrated with polymorphs and occasional monocytes. Round its periphery were deposits of calcium, presumably an old lesion. Sections from the right and left ventricles failed to show evidence of focal inflammation.

Lungs.—Recent ante-mortem thrombosis of the pulmonary veins was observed, probably due to slowing of the circulation by extreme aortic stenosis.

Liver, Spleen.—Passive congestion only.

Kidneys.—These showed an inconspicuous degree of focal embolic nephritis, with scattered foci of interstitial leucocytic infiltration, mostly round cells. Some of the older lesions showed tubular atrophy and interstitial fibrosis.

Adrenals, Lymph Nodes, Bone Marrow, Meninges.—Nothing of note.

Summary of Findings.—Bacterial endocarditis, supervening on chronic rheumatic endocarditis (aortic stenosis and incompetence); mycotic aneurysms of sinuses of Valsalva involving cardiac septa and causing heart-block; infarcts in spleen and right kidney; focal embolic nephritis.

Bacteriological Findings During Life

Isolation of Organism.—Blood cultures on August 18, 19, 23, and 30 in liver broth, liver agar, and glucose broth grew *Br. abortus* within four days. On August 30 there were seven colonies per ml. of blood. Blood cultures of September 23 and November 1 remained sterile during 28 days' incubation.

Identification of Organism.—The organism from the blood culture of August 23 proved to be a Gram-negative non-motile cocco-bacillus, forming colonies 0.5 mm. in diameter after 48 hours' incubation on liver agar in the presence of CO_2. There was no visible growth without CO_2. No acid or gas was produced in lactose, sucrose, dulcitol, maltose, mannitol, glucose, salicin, raffinose, trehalose, arabinose, and xylose. Hydrogen sulphide production on liver-agar slopes was detectable with lead acetate papers for five days. Flood plate cultures of liver agar incubated in the presence of CO_2 showed, on an average of eight tests, a 4-mm. wide zone of inhibition around a paper disk soaked in saturated

aqueous thionine (vital, G. T. Gurr), and no inhibition around a disk soaked in saturated aqueous basic fuchsin. A saline suspension was agglutinated to titre by *Br. abortus* serum (Standards Laboratory, Colindale) and to half-titre by *Br. melitensis* serum. Flood plate cultures on liver agar incubated in the presence of CO_2 showed, on an average of eight tests, a 5-mm. zone of inhibition around a disk soaked in 0.1% aqueous aureomycin, a 12-mm. zone around 0.1% chloramphenicol, and a 4.5-mm. zone around streptomycin 1,000 units per ml.

Thus the organism was a normal strain of *Br. abortus* with normal drug sensitivity.

Serology.—On August 24 the serum of August 23 agglutinated standard *Br. abortus* suspension (Standards Laboratory, Colindale) to a titre of 1/5,000, after 24 hours at 37° C. On May 30, 1950, the serum of September 1, 1949, showed the following agglutinin titres: *Br. abortus* N.C.T.C. No. 5059, non-standard suspension, 1/320; *Br. abortus* homologous strain, non-standard suspension, 1/320; *Br. melitensis* N.C.T.C. No. 5060, non-standard suspension, 1/160 (partial).

Bacteriological Findings After Death

Vegetation.—A portion of the aortic vegetation fixed in formol saline showed very large numbers of Gram-negative cocco-bacilli. The organisms were well demonstrated by over-staining with methyl violet and partial decolorization with aniline water. No intracellular organisms could be seen. A portion of the aortic vegetation, well washed several times in saline and coarsely ground with powdered glass in a mortar, grew a profusion of *Br. abortus* on liver-agar plates during 48 hours' incubation in the presence of CO_2.

Bone Marrow and Spleen.—Cultures taken with precaution to avoid contamination grew *Br. abortus* only.

Blood.—Cultures grew only scanty coliforms and staphylococci.

Drug Sensitivity of Organism.—A comparison of the sensitivities and other characteristics of the strains isolated before and after death with those of N.C.T.C. strains of *Br. abortus* and *Br. melitensis* is set out in Table I. It

TABLE I

Organism:	*Br. abortus*			*Br. melitensis*
Source:	Blood Culture (Patient)	Vegetation (Patient, P.M.)	N.C.T.C. 5059	N.C.T.C. 5060
Growth on liver agar:				
With CO_2:				
24 hours	±	±	±	±
48 ,,	+++	+++	+++	+++
Without CO_2:				
24 hours	0	0	±	±
48 ,,	0	0	+	+++
H_2S production:				
Day 1	+	+	+	0
,, 2	+	+	+	0
,, 3	+	+	+	0
,, 4	+	+	+	0
,, 5	±	±	0	0
Zone of inhibition:				
Thionine (satd.)	3·0 mm.	3·0 mm.	3·0 mm.	0·0 mm.
Fuchsin (satd.)	0·0 ,,	0·0 ,,	0·0 ,,	0·0 ,,
Aureomycin (0·1%)	5·0 ,,	1·0 ,,	5·0 ,,	2·5 ,,
Chloramphenicol (0·1%)	11·0 ,,	4·0 ,,	21·0 ,,	2·5 ,,
Streptomycin (1,000 u./ml.)	4·5 ,,	4·5 ,,	2·5 ,,	2·0 ,,

will be seen that *in vitro* the strain isolated at necropsy was considerably more resistant to both aureomycin and chloramphenicol than that isolated from the blood before treatment.

Comment on Case

There were several unusual features in this case, the most striking perhaps being the well-being of the patient until arthralgia and heart-block occurred. This apparent well-being in the presence of high fever is a feature of uncomplicated Brucella infection, and in this case was unaffected by the presence of a Brucella endocarditis. Only when septal lesions occurred did the patient's condition rapidly deteriorate.

A second noteworthy feature was the failure of penicillin, streptomycin, and aureomycin to alter the course of the disease; indeed, the last-named appeared to precipitate the only symptoms he had during his first stay in the ward. Apparently in spite of therapy his temperature-pulse-respiration chart and general condition slowly improved in a manner not usually seen in other forms of bacterial endocarditis. Physical signs abated rather than increased, and the few doubtful petechiae seen on admission to the ward never recurred. It was this slow and apparently steady improvement in signs and symptoms which lulled us into a sense of false security. The diagnosis of Brucella endocarditis was seriously considered at an early stage in view of the past history of valvular damage and the positive blood cultures; but because of the extreme rarity of this condition and the patient's apparently steady improvement it was not considered very likely until late in the course of the disease.

Clinical Analysis of Published Cases

Comparison with other cases of abortus endocarditis in the literature throws only limited light on the clinical aspect, since, generally speaking, the clinical findings and reports of investigations are scanty. Of the 12 cases* considered, four (including our own) may be regarded as proved beyond doubt (Cases 3, 6, 9, and 10) and the remainder highly probable.

Aetiology and Duration.—All were males. The ages varied from 21 to 61. Occupations were farmer (6), labourer (2), wool-packer (1); in three the occupations were not stated. Death occurred within three to eleven months of the onset of symptoms, and where recorded appears to have been cardiac in type, usually with terminal pulmonary oedema. Embolic and renal deaths, so common in subacute bacterial endocarditis, were not recorded.

Clinical Features.—Aortic regurgitant murmurs were heard in conjunction with a harsh systolic component in six cases; aortic regurgitation with no mention of systolic accompaniment in three. Mitral stenotic murmurs were heard in seven cases. Pericardial friction was twice recorded. Comparison with the necropsy findings (where aortic lesions predominate) makes it seem possible that some of these mitral murmurs were of Austin Flint type; but clinical data, as a whole, are indifferently reported as compared with necropsy findings.

White Blood Cells.—Counts varied from 2,800 to 14,100 per c.mm., with a terminal count of 20,000 per c.mm. in one instance. Neutrophils varied from 66% to 82% of the total.

Chest Radiographs.—Four of the six cases reported showed cardiac enlargement to the left; bilateral bronchiectasis was reported in one, pulmonary infarction in another.

Electrocardiograms.—These were reported in only seven cases—too few and too uninformative to merit

*(1) and (2) Call *et al.* (1944). (3) Hart *et al.* (1951). (4) Quintin and Stalker (1946). (5) Rennie and Young (1936). (6) Rothman (1935). (7) Scott and Saphir (1928). (8) Smith and Curtis (1939). (9) Spink and Nelson (1939). (10) Spink, Titrud, and Kabler (1942). (11) Voth (1949). (12) Wechsler and Gustafson (1942).

detailed description. In four out of six cases shown at necropsy to have aneurysms of the sinuses of Valsalva, there were disturbances of conduction in the form of slurring or notching of the QRS wave (Case 9), delayed A–V condition (Case 1), right bundle-branch block (Case 8), or complete heart-block (Case 3).

Pathological Analysis of Published Cases

In the 12 cases analysed, certain morbid anatomical features recur too frequently to be dismissed as coincidental, and taken together may be considered to constitute a fairly characteristic type of lesion.

Weight of Heart.—This was not recorded in three cases; otherwise it was significantly increased, varying from 465 to 646 g. It is probably relevant to note that in all nine cases there was an aortic valvulitis, old or recent.

Previous Valvular Lesions.—As in the case of subacute bacterial endocarditis the vegetations generally occurred on a valve rendered abnormal by previous disease or congenital malformation. Antecedent rheumatic valvulitis was either diagnosed during life or demonstrated at necropsy in seven cases (Nos. 1, 2, 3, 4, 7, 8, and 10), while two others showed a bicuspid aortic valve (Cases 11 and 12). In this connexion it is worth recalling the evidence presented by Gross (1937), who suggested that most bicuspid aortic valves are not congenital anomalies but the result of healed rheumatism.

Fibrosis and Calcification.—Fibrous thickening of the affected cusp was present in all 12 cases, with added calcification in eight. Doubtless this was largely due to old rheumatism, but it has been pointed out by Libman and Friedberg (1948) that in prolonged subacute bacterial endocarditis both these phenomena may be found as evidence of healing.

Valves Affected.—These were (*a*) aortic alone in eight cases (Nos. 1, 3, 4, 6, 8, 9, 11, and 12); (*b*) mitral alone in two cases (Nos. 5 and 10); and (*c*) aortic and mitral in two cases (Nos. 2 and 7). In group (*a*) one case (No. 11) showed a calcified mitral valve without vegetations, while in group (*b*) there was one uncomplicated aortic stenosis (Case 10).

Aneurysm of Sinus of Valsalva.—In no fewer than six of the twelve cases (Nos. 1, 3, 8, 9, 11, and 12) aneurysmal dilatation of the sinuses of Valsalva was recorded, with spread of the infection through the aortic wall into the auricular septum (Cases 8 and 12), the ventricular septum (Cases 3 and 9), the myocardium (Case 11), or the pericardial sac causing fatal haemopericardium (Case 1). It is known that aneurysms of the sinuses of Valsalva may complicate aortic lesions in subacute bacterial endocarditis, with rupture into the pericardium (Libman and Friedberg, 1948), or into the septa causing bundle-branch block (Rothschild, Sacks, and Libman, 1927), but nowhere do the authorities quoted suggest that such accidents are other than very rare.

Tricuspid Ulceration.—The extreme rarity of tricuspid valvulitis makes its incidence in four cases a notable observation (Cases 3, 8, 9, and 12). In all four infection had spread from the sinuses of Valsalva through the aortic wall and cardiac septa to involve the medial leaflet of the tricuspid valve.

Myocarditis.—Focal myocarditis was observed in six cases (Nos. 1, 2, 4, 6, 10, and 12), usually in the form of groups of necrotic myocardial fibres, with aggregations of leucocytes and fibroblasts. In Case 4 infective emboli from the aortic vegetations had given rise to mycotic aneurysms along the line of the coronary arteries.

Infarcts.—These were recorded in the following organs: spleen, 9; kidneys, 3; and lungs, 1.

Nephritis.—In seven cases (Nos. 1, 2, 3, 4, 5, 6, and 12) a renal lesion of some sort was present, though the nomenclature employed is variable and includes such terms as "glomerulo-nephritis" (6), "toxic glomerulo-nephritis" (1), "subacute nephritis" (2), "diffuse subacute pyelo-nephritis" (4), and "acute interstitial nephritis" (12). Our own case showed a mild form of focal embolic nephritis, but in none of the case records was a typical "flea-bitten" kidney described.

Comparison with Brucella (Melitensis) Endocarditis

Eight case records* of endocarditis due to *Br. melitensis* have been analysed for the sake of comparison. Again only males were affected, but there were significant differences in the pathological picture. In Table II the incidence of the various features is given. It should be stressed that the case records are scanty in comparison with abortus endocarditis.

TABLE II

	Abortus	Melitensis
Previous lesion	9/12 (75%)	Nil
Aortic valve	10/12 (83%)	4/8 (50%)
Mitral valve	4/12 (33%)	4/8 (50%)
Fibrosis	12/12 (100%)	4/8 (50%)
Calcification	8/12 (67%)	1/8 (12%)
Aneurysm of sinus of Valsalva	6/12 (50%)	1/8 (12%)
Septal involvement	5/12 (42%)	Nil
Tricuspid ulceration	4/12 (33%)	"
Acute myocarditis	6/12 (50%)	"
Nephritis	7/12 (58%)	2/8 (25%)
Infarcts	9/12 (75%)	2/8 (25%)

Discussion

The foregoing data indicate that *Br. abortus* endocarditis is a distinct entity with certain characteristic features. Occurring predominantly in the male sex, the disease runs a slow and, until the present, fatal course, death occurring within three to eleven months of the onset of symptoms. More often than not there is a previous history of a heart damaged by rheumatism or a congenital abnormality.

So far the disease resembles subacute endocarditis due to a non-haemolytic streptococcus, although the sex incidence in Brucella endocarditis is more striking than in subacute bacterial endocarditis. In the latter the M/F ratio is only 3:2 (Blumer, 1923), whereas all the recorded cases of the former have been in males. The nature of the patient's occupation is not in itself a sufficient explanation of this fact, since female farm-workers drink the same milk and are also prone to uncomplicated brucellosis.

It is difficult to assess the significance of the frequency of aortic lesions in such a small series, but it is clearly aortic valvulitis which produces the most typical cardiac lesions. The tendency to ulceration of the surrounding tissues leads to mycotic aneurysms of the sinuses of Valsalva, resulting in septal myocarditis, tricuspid ulceration, or haemopericardium. The frequency of septal involvement greatly exceeds

*(1) Casanova and d'Ignazio (1933). (2) De la Chapelle (1929). (3) Gounelle and Warter (1935). (4–7) Hughes (1897, Cases 5, 8, 11, and 13). (8) Levy and Singerman (1938).

other forms of bacterial endocarditis, and the lesions are large compared with those seen in streptococcal subacute bacterial endocarditis, in which gross suppuration is absent (Bracht and Wächter, 1909).

The few electrocardiograms reported in cases of Brucella endocarditis show some disturbances of conduction, and it seems likely that these are related to septal lesions. Brucellosis *without* endocarditis may be accompanied by electrocardiographic changes in the form of elevation or depression of the RS–T interval, and low isoelectric or inverted T waves (Rubegni, 1939); however, these changes rapidly revert to normal as the fever and symptoms abate, though Friedberg (1949) has reported a case with inversion of T waves for two months after.

The defects in conduction noted in our own case and in Cases 1, 8, and 9 (the lesion in each case being aortic) have not been recorded in uncomplicated brucellosis, and are extremely rare in streptococcal subacute bacterial endocarditis. Libman and Friedberg (1948) reported prolongation of the P–R interval to 0.21–0.36 second in 15% of cases of subacute bacterial endocarditis, but state that the QRS phase is rarely widened in this disease, and that bundle-branch block was noted in only one of their series of 109 cases, due to pressure of a bacterial aneurysm of the sinus Valsalva on the interventricular septum. Complete heart-block, according to the same authors (p. 346) has been reported, but was not seen in their series. White (1944) states that very rarely in subacute bacterial endocarditis aneurysm or perforation of the ventricular septum may occur, and that again very rarely the A–V bundle of His may be affected, causing heart-block. Katz (1946) points out that anaemia and the underlying rheumatic process may affect the electrocardiographic picture in subacute bacterial endocarditis.

The paucity of case records in four of the melitensis series makes clinical comparisons difficult and some of the negative findings of doubtful value. In Hughes's cases, for example, the issue of previous heart disease was never really raised, and it is difficult to assess the significance of fibrosis of the valves in four out of the eight cases, especially in what is essentially a chronic inflammatory process. On the other hand, only one of the melitensis cases showed an aneurysm of the sinuses of Valsalva; and septal involvement, tricuspid ulceration, and acute myocarditis—three features which give an independent character to the lesion of abortus infections—were not observed. Only one case of suis endocarditis is recorded (De Gowin *et al.*, 1945), and that in a male with no previous history of rheumatism who died in the seventh month of his illness of haemorrhage from a mycotic aneurysm of the femoral artery. Necropsy revealed aortic vegetations with ulceration and focal myocarditis. The E.C.G. revealed left axis deviation and increasing negativity of T3. The kidneys showed diffuse nephritis and chronic granulomata.

There seems to be a greater tendency to gross infarction of other organs in abortus endocarditis than in either the streptococcal subacute bacterial or the melitensis forms. The accounts of the concomitant nephritis in abortus endocarditis are very variable, but the condition is presumably of focal embolic origin.

All the antibiotics used in our case failed to control the disease, perhaps because dosage was discontinued too soon, but Spink *et al.* (1948) reported a case in which *Br. abortus* was isolated from the blood during life after 118 g. of streptomycin had been given over a period of 31 days; at necropsy, however, positive cultures could not be obtained, although aortic vegetations were present. With the newer antibiotics such cases may be seen more often in the future.

Summary

The literature of Brucella endocarditis has been reviewed and the case records analysed. A new case of *Br. abortus* endocarditis is reported.

All cases of Brucella endocarditis, whether abortus, melitensis, or suis, have been in males.

Br. abortus endocarditis is a distinct clinico-pathological entity, with a duration of three to eleven months. Death in all the recorded cases has been a cardiac one, usually with marked pulmonary oedema.

The frequency of myocardial lesions, especially in the cardiac septa, where they give rise to disturbances of conduction, appears to set abortus endocarditis apart from other forms of bacterial endocarditis, including melitensis infections.

Aortic lesions predominate in abortus endocarditis. In both melitensis and abortus endocarditis, aneurysms of the sinuses of Valsalva, septal involvement, and heart-block have occurred only with aortic lesions. To date only one case of *Br. suis* endocarditis has been reported.

There is no clear evidence that the use of antibiotics has so far altered the course of the disease. Aureomycin, streptomycin, penicillin, and chloramphenicol in short courses all failed to benefit our own case.

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THE REDUCTION OF SURGICAL HAEMORRHAGE

SOME OBSERVATIONS ON CONTROLLED HYPOTENSION WITH METHONIUM COMPOUNDS

BY

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The literature of the methonium compounds has grown considerably during the past two years. The pharmacology and the physiological action of the group have been fully discussed by Paton and Zaimis (1948, 1949). Decamethonium as a relaxant was introduced by Organe in 1949. Other publications have followed, notably one by Hunter in October, 1950. The hypotensive action of the "middle" numbers of the group, first indicated by Organe when studying pentamethonium as an antidote to decamethonium, has been exploited by several workers in the treatment of hypertension (Campbell and Robertson, 1950; Turner, 1950; Saville, 1950). The action of hexamethonium on gastric secretion has been reported upon by Kay and Smith (1950), as well as by other workers. Armstrong Davison (1950) and Enderby (1950) have reported on the use of drugs of the group to produce hypotension during surgery in order to obtain reduced bleeding.

It is my belief that many anaesthetists are now using the methonium compounds for this last purpose, and I feel that many of us are working in ignorance of the experience and results of our colleagues. Since Enderby and I demonstrated the technique of producing hypotension during an operation at a meeting of the Society of Anaesthetists of the South-west Metropolitan Hospital Region at Winchester in May, 1950, we have received many inquiries about the technique and the use of the methonium drugs. This correspondence suggests that many anaesthetists may be groping along the dark passages already traversed by those of us who have been using the technique for some time. I do not claim to have reached daylight myself as yet, but in the hope that the results of my experience, and those of my colleagues in the plastic unit, may be helpful to others, and stimulate research into what may prove a useful field of activity, I venture to record certain clinical impressions that I have gained during a year's growing familiarity with the use of the methonium compounds to reduce surgical bleeding.

The idea of lowering the blood pressure during surgery, and so reduce bleeding, was introduced to us in this country by Griffiths and Gillies in 1948, and further amplified by Gillies in his Clover Lectures to the Faculty of Anaesthetists in 1950. These workers in Edinburgh achieved hypotension by using the total spinal technique. By this technique they have shown that considerable falls in blood pressure may be produced by spinal block high enough to paralyse the thoracic sympathetic. They also showed that an adequate circulation can be maintained with considerable hypotension present (60 mm. of Hg, for instance), given full oxygenation and vasodilatation. After examining the results of investigations of the action of tetraethylammonium chloride, and the two methonium compounds, hexamethonium and pentamethonium, Enderby suggested to us at the Plastic Unit at Rooksdown House that these drugs might be used as an alternative to the total spinal technique. It must be realized that the autonomic ganglion block produced by these drugs is unselective, and that a combined sympathetic and parasympathetic paralysis is obtained. It was quickly realized that the effect was considerably influenced by the position of the patient, and that the hypotension produced was partly postural.

Choice of Drug

Previous work having shown that pentamethonium was slightly more effective in producing hypotension than the tetraethylammonium, it was with the methonium compound that we began to work. For fully three-quarters of the cases done by me personally, pentamethonium iodide has been used. Latterly hexamethonium bromide has become the drug of choice, it being my impression that this member of the group is slightly more certain in its action. It has been suggested by one of my colleagues that the hypotensive action of pentamethonium is enhanced if decamethonium has been used for relaxation during intubation or early in the anaesthetic; I have no personal experience of this combination.

Dosage.—In the early days small initial doses were the rule, 10 mg., followed by another 10 or 20 mg. after a period of observation, being used; but as time went on, and our confidence grew, we increased the initial dose, finding much greater certainty with no added worries, until I now regularly employ 50 mg. initially for a healthy adult. Additional dosage to maintain hypotension is dictated solely by circumstances and no hard-and-fast rules can be laid down. If the pressure rises to 75 or 80 mm. half the initial dose should be given. This may be repeated at intervals throughout the operation. One has learned to identify certain types of individual who are particularly sensitive to the drug, and who will ride comfortably with satisfactory hypotension for an hour or more on an initial dose of 10 mg.

Suitable Cases

Type of Operation.—As hypotension is to a large extent postural and depends on the pooling of the blood in the dilated vessels, especially those of the legs, operations in which a foot-down tilt can be maintained are most suitable for the employment of this technique. For maximum success the surgical site should be elevated above the pelvis and legs. Thus operations on the head and neck, thorax, etc., have produced the most satisfactory results. Examples of such are a thyroidectomy, a large scalp rotation flap, and a mastectomy—all potentially "bloody" performances. In each of the three cases bleeding was minimal. The thyroid resembled a demonstration of anatomical dissection, the scalp-flap lower towel was almost dry at the end of the operation, and in the case of the mastectomy the towel below the axilla was devoid of its usual post-operative pool of blood.

Posture, however, is not everything, and considerable success has been achieved with patients in the lithotomy position for repair of the pelvic floor. (It is hoped to record this series in a separate communication.)

Type of Individual.—Patients with mild hypertension (say 180/100 mm. Hg) react very readily. As an initial dose 10 mg. of pentamethonium iodide may produce adequate hypotension (and a bloodless field) in a pelvic floor repair lasting 40 minutes. If the optimum

position is obtainable all types of individuals will respond, though tough, heavy, imperturbable males are inclined to be resistant and disappointing. I have so far had no experience of the technique with children.

Technique

Premedication may be according to taste. Personal preference is for "omnopon"-scopolamine. (Note the patient's pre-operative blood pressure, and any alteration under premedication. A marked fall denotes a probable sensitive reactor to methonium compounds.) Induction is with thiopentone or other barbiturate, followed by nitrous-oxide–oxygen, with or without cyclopropane to settle. Intubation can be carried out with or without a relaxant. As soon as composed, the patient should be tilted into a 20-degrees foot-down position. A Gordh needle, or a needle with a leak-proof cock, should be placed in a suitable vein, and the initial dose of pentamethonium iodide (or hexamethonium bromide) given. A sequence of blood-pressure readings are now taken. When the systolic reading is in the neighbourhood of 70 mm. or below (and not higher than 80 mm.), the surgeon may begin work. The fall to the necessary level usually takes place in three to five minutes. If subsequent movement of the patient is necessary to get an ideal operating position the blood pressure must be watched. If there is a rise further dosage of the methonium may be given, unless it can be lowered by slightly increasing the foot-down tilt. Maintenance of anaesthesia is usually with nitrous oxide and oxygen supplemented with a barbiturate, pethidine, or cyclopropane. The giving of small quantities of barbiturate in weak solution during profound hypotension does not seem to have any further effect on the blood pressure. I have usually avoided cyclopropane, owing to its occasional tendency to produce mild hyperpiesis.

The usual aim is to keep the systolic pressure between 60 and 70 mm. For the first half-hour or longer this is generally easy. If it falls below 50 mm., reducing the foot-down tilt will tend to raise it. The diastolic reading is often difficult to record accurately. In operations lasting from one-half to three-quarters of an hour the initial dose of the drug will usually prove sufficient. In longer operations additions of from 10 to 25 mg. of the drug may have to be given. Often increasing the table-tilt will prolong the action of a dose. There seems little benefit in lowering the systolic pressure below 60 mm. So far the longest period of maintained hypotension of 60 mm. has been 2½ hours. This was an extensive scalp-plastic operation in a woman of 38. She suffered no ill effects, her cerebral and renal functions subsequently being normal.

The blood pressure, either by posture alone or with the addition of further methonium, must be kept low until the skin is closed. Thereafter the patient should be raised to the horizontal and the blood pressure watched. If there is not a rise to above 80 mm. systolic, a slight head-down tilt may be adopted for two to three minutes. This will generally produce a rise to about 100 mm. systolic. If, however, the systolic pressure still remains below 80 mm., 10 mg. of "methedrine" will always raise it in from one to three minutes.

One word of warning here is necessary. If the lithotomy position has been adopted (as for a pelvic floor repair) and the blood pressure has been held satisfactorily low, care must be taken when the legs are lowered. Flow of blood into the legs may produce a further drop of pressure, and a head-down position must be adopted at once.

Post-operative Phase

Great care must be taken in the immediate post-operative stage. The patient must be lifted flat on to the stretcher, and kept so on the way back to the ward. He must be wheeled head downhill on ramps or inclines, and lifted into bed with care to avoid raising the head and shoulders. The foot of the bed must be kept up on blocks until the anaesthetist has again seen the patient. The blood pressure is usually steady at 100–110 mm. in about two hours. No particular precautions are necessary after the blood pressure is stabilized. It usually returns to normal in 24 to 36 hours. Dilated pupils sometimes last for two days, rarely leading to a complaint of difficulty in reading during the first day. One of our cases had a very low temperature—95.6° F. (35.3° C.)—for six hours after operation. Vomiting was very slight, as one might expect after gas–barbiturate anaesthesia. My impression is that it was even less than usual. A few patients have complained of tiredness and lassitude for the first day. No major ill effects have been noted. There has been no case of prolonged hypotension, and no case of cerebral damage or alteration in function.

Dangers

The obvious dangers might seem to be: (1) Reducing the cerebral circulation below a safe level. In hyperpietics the sudden fall in blood pressure and diminution of circulation might be specially dangerous. (2) Ill effects of reduced circulation on other organs—for example, kidneys. (3) *Prolonged* effects of hypotension (4) Post-operative secondary haemorrhage as the blood pressure rises again. (5) Danger during the unstable immediate post-operative stage; especially during transport and lifting into bed, etc. (6) Failure to establish hypotension initially or to maintain it throughout the operation, leaving the patient deprived of normal vascular tone and liable to increase bleeding.

Cautious approach to the subject suggests that these dangers are mostly theoretical. With full oxygenation of the blood, with vasodilatation as a result of the sympathetic block, and with a constant blood volume, sufficient circulation is maintained to prevent any organ falling into jeopardy. Even two and half hours with the systolic pressure below 60 mm. produced no subsequent alteration in function. Post-operative secondary haemorrhage has been conspicuously absent; in fact, we have seen it only once, and that in a forehead-flap rhinoplasty—a procedure which under other conditions has been known to lead to bleeding after operation. If methylamphetamine hydrochloride ("methedrine") has been given I suggest that the danger of subsequent haemorrhage is greater after the sudden rise in pressure which results. When a normal blood pressure is regained gradually the danger seems remote.

Danger during the movement after operation is very real. It is worth while here to repeat the warning already given. To ensure safety, some responsible and instructed person from theatre or ward must accompany the patient, and the blood pressure must be recorded immediately on his regaining the bed, and thereafter half-hourly. Methylamphetamine hydrochloride should be at hand, and be given in 10-mg. doses

if hypotension is prolonged. (In practice this has very rarely been necessary.)

Failure to achieve sufficient hypotension, or to maintain it, after autonomic ganglion block may lead to trouble. If bleeding appears to be severe, replacement therapy is the only measure likely to remove the danger to the patient. Fortunately, failure in suitably chosen cases is infrequent, and the results of failure are rarely serious. I personally have been worried by severe bleeding once only.

Summary

The production of hypotension during surgical operation by blocking the autonomic ganglion with a suitable methonium drug can produce operating conditions of great attraction to the surgeon, can considerably reduce bleeding and therefore add to the patient's safety and post-operative health, and seems to be a safe procedure in skilled hands and with constant observation. It must be realized that posture plays a large part in producing the desired level of hypotension, and therefore the technique is unsuitable for certain operations. Some individuals also appear unsuitable, and the individual reaction to the drugs used so far is variable.

It must be mentioned that success, or otherwise, in reducing haemorrhage in each individual case has been assessed entirely by the surgeon. Well over three-quarters of the 250 cases have been categorized as "good."

ADDENDUM

Since this paper was completed the subject has been debated at a meeting of the Anaesthetic Section of the Royal Society of Medicine, with papers from Drs. Enderby and Armstrong Davison. Although the work already done in this field is consequently more widely known, I feel that attention to the basic principles of the technique and the importance of careful selection of suitable cases cannot be overemphasized.

Recently a case has been brought to my notice where a patient died two days after an operation for removal of a malignant tumour involving skull and meninges. Hexamethonium bromide had been used to control severe haemorrhage. The patient's blood pressure apparently never rose above 80 mm. systolic during the two post-operative days, nor was any adequate attempt made to raise it. Anuria was absolute for the first 24 hours, but the kidneys excreted some urine during the second 24 hours. Two errors of technique seemed to me to have been made in this case. First, the drug was used late to control already established haemorrhage, instead of at the beginning to prevent bleeding. It is possible that the circulating blood volume had already been dangerously reduced by the time it was used. Secondly, hypotension was allowed to persist for too long without attempts to correct it by posture and methylamphetamine hydrochloride. I think it is absolutely essential, in using this technique, to maintain a full circulating blood volume and full oxygenation, and to use an adequate dose of the drug to produce successful block and consequent vasodilatation. If extreme hypotension is prolonged beyond a few hours, measures must be taken to correct it.

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TUBERCULOUS LYMPHADENITIS IN THE NIGERIAN AFRICAN

BY

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Old-established conceptions of the pathogenesis of tuberculous lymphadenitis still appear to hold the field. Thus Boyd (1947) states that the cervical lymph nodes may become infected through one of two routes: either by the blood stream, in which case scattered nodes are attacked, or by the lymph stream. In the latter, which is much the commoner mode of infection and accounts for 90% of cases, the cervical nodes become involved via the lymphatics from a primary tuberculous focus in the tonsils, adenoids, or teeth caused by ingestion of contaminated material, notably milk from tuberculous cows.

Mitchell (1917), in Edinburgh, found 88% of cases of tuberculous adenitis in children to be due to the bovine bacillus, and demonstrated tubercle bacilli in 20% of samples of the local milk supply. In New York, Park (1910) found 34% of all cases, and 54% in children under 5, to be of bovine origin. In corroboration of the path of infection microscopical evidence of tuberculosis in the tonsils has been reported in 38% of cases, while tubercle bacilli have been demonstrated in the decayed dental root pulp of those harbouring tuberculous nodes. It should, however, be pointed out that the discovery of a tuberculous focus in a tonsil is by no means proof positive that this was the original portal of entry. A lymphatic organ such as the tonsil, endowed with generous lymphatic communications, might conceivably undergo retrograde infection from previously tuberculous cervical nodes.

There seems, however, to be considerable support for this conception in the case of bovine infection, though it does not appear to be applicable to all cases of tuberculous lymphadenitis. In civilized countries an increasing attention to the care of herds and to pasteurization has of recent years considerably reduced the proportion of cases attributable to bovine infection. In Southern Nigeria bovine infection is a rarity, but for a different reason. Relatively few cattle are driven down from the north, because tsetse belts have to be traversed *en route*, while fresh milk and butter do not enter into the dietary of Southern Nigerians. Peripheral tuberculous lymphadenitis among the latter may thus be taken as almost invariably due to infection with the human bacillus.

Some observations on the features of the disease in 51 consecutive cases seen in Lagos are here presented and the implications discussed. In 24 cases the diagnosis was made on clinical grounds alone, always quite typical, and in the majority with associated sinuses, cold abscess, pulmonary tuberculosis, or pleural effusion. In five cases the diagnosis was supported bacteriologically by gland puncture, in 10 cases histologically by gland biopsy, and in 12 by the macroscopic appearance at surgical excision with additional histological confirmation in five. Tuberculin tests were not carried out in this series.

Clinical Data of Present Series

Of the 51 cases 32 were male and 19 female; by European standards a relatively large number were

adult, 17 (33.3%) being over 20 (see Table). Inquiry was made whether there had been any recent death in the patient's household, or whether any member suffered from persistent cough with expectoration or from enlarged lymph glands; but in only two cases was any possible evidence of a recent tuberculous association elicited. One stated that a brother had died two years previously at the age of 14 suffering from cough, another that two members of his family had enlarged lymph glands similar to his own. Twenty-seven of the patients took their food by dipping their fingers into a communal family food-bowl; the remaining 24 ate from a separate plate. Twenty-eight patients from time to time consumed tinned milk, and eight of these also on occasion had cold-store butter, but only two admitted to the consumption of fresh milk.

Details of Cases

Age Group:	0–4	5–9	10–14	15–19	20–29	30–39	40 and Over	Total
Male	2	8	7	6	6	2	1	32
Female	4	3	3	1	6	1	1	19
Total ..	6	11	10	7	12	3	2	51
Associated dental or faucial sepsis	—	—	—	—	2	2	—	4
Associated trouble with dentition	—	2	—	—	—	—	—	2
Associated lactation	—	—	—	—	2	1	—	3
Radiological evidence of old pulmonary or hilar gland focus	1 (17%)	3 (27%)	3 (30%)	3 (43%)	5 (42%)	2 (66%)	1 (50%)	18 (35%)
Ditto in 100 controls	10%		22%		28%	24%		21%
Cold abscess and/or sinuses ..	1	1	3	4	4	1	2	16
Coincident pulmonary tuberculosis ..	1	—	—	—	2	—	—	3
Pleural effusion	1	—	1	—	—	—	—	2
Tuberculous meningitis ..	—	1	—	—	—	—	—	1
Enlarged thymus	1	3	—	—	—	—	—	4

In contrast to this lack of any recent source of tuberculous infection, in four cases the onset of an upper cervical or submaxillary lymphadenitis was definitely associated with a homolateral dental or alveolar infection; in three cases an axillary adenitis was unmistakably connected with lactation; and in two cases a troublesome erupting tooth clearly heralded the onset of a submaxillary adenitis. In 14 other cases there was coincident dentition, but no such close and clear causal connexion between the latter and the lymphadenitis. Radiological evidence of a pre-existing primary complex, or calcified foci in lungs or hilar glands, was found in 35% of all cases, as opposed to 21% in a series of 100 comparable controls.

As regards the physical findings, it is notable that more than one group of glands was involved in 30 of the 51 cases. Although various groups might become affected in rapid succession, as a rule one group was primarily involved, with subsequent spread at intervals and in lymphatic continuity to other groups. Groups are defined broadly as cervical, axillary, or inguinal; and unilateral involvement of submaxillary, jugular, accessory, and supraclavicular glands is classified as disease of one group only. In a proportion of cases there was, in addition to the glands manifestly tuberculous, a slight or shotty enlargement of glands in other, remoter groups; it was thought that this was probably in the nature of a focal reaction to products of the tubercle bacillus rather than an active tuberculous infection.

Although the cervical glands were most often initially affected, the axillary glands were primarily involved in seven cases, and involved secondarily and in conjunction with other groups in a further 12, while the inguinal glands were the primary offenders in three instances and secondarily involved in another three.

Any type or degree of the disease might be met with at any age. In children under 5, however, there was a tendency to a very massive bilateral cervical glandular enlargement, giving a bull-necked appearance, often with oedema of the superficial cervical tissues, and sometimes with an associated axillary lymphadenitis. This type appears to reflect a rapidly developed and marked sensitization to the products of the tubercle bacillus, possibly the result of an early and heavy primary infection. The general condition of these children was, however, usually fairly good and the response to conservative lines of treatment slow but satisfactory.

Cold abscess and sinus formation, which were noted in 16 cases, occurred in the younger age groups as a rule only after fairly prolonged disease, but often in the older age groups after disease of much shorter duration.

There was coincident pulmonary tuberculosis in three cases—bronchopneumonic in patients aged 3 and 24, and upper lobar and probably pneumonic in one aged 27. While the later cavitative type of pulmonary tuberculosis is not associated with a lymphadenopathy, the bronchopneumonic and pneumonic types almost always are. Thus no case presenting with tuberculous lymphadenitis must be judged simple and of good prognosis until associated pulmonary disease has been excluded.

Two children, aged 4½ and 12, had coincident pleural effusions. One child aged 6, who had apparent meningeal involvement when first seen, developed a hemiplegia and died within a few days. Four children under 10 had greatly enlarged thymuses.

Treatment

Most cases without sinus formation responded very favourably but with varying celerity to conservative measures, a full nutritious diet, cod-liver oil or calciferol, and occasionally a period of rest in hospital. Cold abscesses might require aspiration. In the presence of sinuses response to conservative treatment was slow and unsatisfactory, and if only one gland group was involved complete surgical excision was found to be most successful. Such excision was carried out in 12 of these 51 cases because of sinus formation or slow response to conservative measures, or because of involvement of a small localized gland group. While in the majority healing was prompt, in a few cases areas of tuberculous ulceration in the scar led to more protracted but eventually sound healing. Surgical measures of less extent were never employed.

While the immediate results of surgical excision are excellent, it should be remembered that the period of sensitization of the lymph glands may be prolonged, and that after complete eradication of the involved gland group other groups may show the disease months or years later. Thus one patient in this series, for whom I had performed a complete left cervical clearance over two years previously, returned with tuberculosis of the upper right cervical glands with one cold abscess. The recurrence was of recent origin and responded well to conservative measures. In the chronic case with involvement of many gland groups, multiple sinuses, cold abscesses, secondary infection, and general debilitation,

surgery is excluded, conservative treatment often fruitless, and the course usually progressively downhill.

Discussion and Conclusions

It is apparent that clinical tuberculous lymphadenitis does not represent a primary infection with the organism. The glandular component of a pulmonary primary complex consists of a very limited enlargement and caseation of only those few nodes directly draining the lung focus, for the lymphatic glands have as yet acquired no sensitization to the products of the tubercle bacillus. On the other hand, the glandular enlargement of a clinical tuberculous lymphadenopathy, which may be very considerable or even massive and involve a whole group or several groups of glands, indicates that a degree of such allergy has now developed. The time that must elapse between the primary infection and full development of sensitization varies, possibly according to the dosage of the initial infection, but may be fairly short, as suggested by a case in this series that first exhibited lymphadenopathy at the age of 18 months. Once allergy is attained, the interval before it again wanes and desensitization is achieved is also variable. Thus three patients had cervical scars, attributed by them to incision or enucleation of tuberculous glands by native "doctors" five, six, and seven years earlier respectively, and this probably represents about the longest duration of sustained glandular sensitization.

The source and route of the primary sensitizing infection merit consideration. Despite the absence of milk and milk products from the dietary, the use of the communal food-bowl offers a possible alternative mode of infection by ingestion in 27 of the 51 cases. That the alimentary route is not the probable one is suggested by the comparative rarity of primary abdominal tuberculosis and the infrequency of calcified abdominal glands radiologically. The likely mode of infection is then by inhalation, though whether the portal of entry is nasopharyngeal or pulmonary remains open to question.

Examination of the tonsils for tuberculous foci has not yet been carried out in Southern Nigeria. From a pulmonary primary focus bacilli could pass via the hilar and broncho-mediastinal glands to the cervical glands and even further afield to the axillary nodes. It would be necessary to assume, however, in those rarer cases in which the inguinal glands are primarily involved, that infection had been, exceptionally, by ingestion and not by inhalation, and the route of infection via the ileo-caecal, para-aortic, and iliac nodes. Such an explanation would yet fail to account for those instances in which the inguinal glands are involved in association with the axillary and/or cervical glands.

The final possible method of spread of infection from the primary complex to the peripheral lymph nodes is by the blood stream, a route too little considered in the past, paralleled in such diseases as syphilis, and consistent with the early bacteriaemia that has been shown to occur in tuberculous infection. Though proof is lacking, this last route seems to be the most convincing possibility. Once deposited in the glands, the bacilli may be demolished, may be permanently latent if the degree of glandular sensitization never attains the threshold requisite for the occurrence of manifest disease, or, if this threshold is exceeded, may lie latent only until and if some precipitating factor provokes overt tuberculous lymphadenitis.

The precipitating factor is probably not a further tuberculous infection. In this series a history of a recent tuberculous contact was notably rare, but in no fewer than nine cases there was a clear and unmistakable precipitation of the disease by lactation, a troublesome erupting tooth, or a pyogenic dental or alveolar infection. Admittedly there remain 42 cases in which no such factor is evident. It is probable that in very young children with a high degree of allergy the provocative agent may be so trivial as to be easily overlooked—normal dentition, perhaps. Further, in some cases the precipitating factor might conceivably be general rather than local—for instance, an attack of malaria. Though no such case occurred in this series, I have observed on several occasions the association of a deficiency syndrome (probably of protein and the vitamin-B complex), characterized by weakness, skin changes, severe anaemia, and oedema, with tuberculous lymphadenopathy.

The cervical glands, which are those most commonly affected by tuberculosis, are also those most prone to intercurrent non-tuberculous infection from ears, pharynx, tonsils, and teeth; while for the axillary glands lactation, and for the inguinal chiggers, tropical ulcer, or venereal disease, may pull the trigger. Once one group of glands has been thus excited to overt tuberculous disease other adjacent groups may be affected by lymphatic channels and in lymphatic continuity.

Summary

A survey of 51 cases of tuberculous lymphadenitis in the Nigerian African is made. It is pointed out that there is a tendency to rather more florid manifestations than in the European, that in a high proportion of cases more than one gland group is involved, and that the axillary glands are quite often, and the inguinal glands not rarely, those primarily affected. Certain suggestions are made regarding the pathogenesis of the disease.

I should like to express my thanks to Dr. G. B. Walker, Director of Medical Services for Nigeria, for permission to publish this paper.

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At this season of the year, when Continental travel is likely to be popular, there are certain insurance aspects which should be carefully considered. It is possible, the insurance company having been informed beforehand about the precise period of the Continental visit, for the normal motor policy cover to be extended for use on the Continent. Some companies will include under this heading the Marine Transit risk, but inquiry should be made specifically upon this point. Certain countries on the Continent, such as Norway, Sweden, Denmark, and Switzerland, require specific information to appear on a certificate of insurance. In the event of a visit to these countries the insurance company will require details of the engine and chassis numbers of the car and a note stating inclusive dates of the proposed visit. It should be noted that the cover granted by the comprehensive motor insurance policy for personal effects is somewhat limited, and, while the detail varies a little as between companies, as a rule it extends only to a total of £20. Experience has shown that for Continental travel this amount is inadequate, and those who intend to have a holiday abroad are strongly recommended to take out a separate insurance to the full value of the effects which they propose to take with them. A specially attractive policy of this type can be obtained through the Medical Insurance Agency, B.M.A. House, Tavistock Square, London, W.C.1, or 6, Drumsheugh Gardens, Edinburgh.

HEREDITARY HAEMORRHAGIC TELANGIECTASIA WITH HEPATOSPLENOMEGALY AND ASCITES

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Since Osler (1901) distinguished hereditary haemorrhagic telangiectasia from other hereditary bleeding diatheses, it has often been described, and has been found to be associated with familial epistaxis, melaena (Gambill, 1946), haematemesis, haematuria, pulmonary arteriovenous fistula (Moyer and Ackerman, 1948), profound anaemia, and splenic or liver enlargement (Roles, 1928; Fitz-Hugh, 1931; van Bogaert and Scherer, 1935). Anning, in a personal communication, states that hepatomegaly has not been noted in any of the cases of Garland and Anning (1950a, 1950b) and that the splenic enlargement is usually thought to accompany severe anaemia. None of 56 patients recorded by Garland in 1936 had evidence of liver disorder. Nora Schuster (1937) published a case of telangiectasia with splenomegaly in which there were multiple aneurysms of the splenic artery. She refers to five complete necropsies, in four of which the spleen was enlarged but not the liver. In two cases of Fitz-Hugh there was atrophic necrosis of the liver after transfusion intolerance. Another showed fatty change, haemorrhage, and biliary dilatation, and her own case showed venous congestion and patchy periportal and peribiliary fibrosis, the patient having died with heart failure. The necropsy on van Bogaert and Scherer's case was the only one in which a true cirrhosis was present. They described the case of a patient with familial telangiectasia and a true Laennec's cirrhosis whose mother also had hepatomegaly. Saksela *et al.* (1949) stated that Rooschüz (1937) was the first to diagnose atypical liver cirrhosis at necropsy, and that Johnson and Nordenson (1942) were able to find some sort of functional disorder of the liver in at least one test in all cases. Parkes Weber (1936) thought that the liver changes might be the result of dysbiotrophy. He referred to two further necropsies without detail.

The present report is of a patient with the Osler–Weber–Rendu syndrome, severe anaemia, nose-bleeding and intestinal bleeding, together with hepatosplenomegaly and ascites. The latter is assumed to be the result of cirrhosis of the liver as described by van Bogaert and Scherer. Ascites is not commonly noted, but has been described by Gurney Yates (Hurst and Plummer, 1932).

Case Report

A woman aged 63 was admitted to hospital on April 5, 1950, with gross anaemia, telangiectasia, ascites, and hepatosplenomegaly. Neither her two older sisters nor her parents were similarly affected. Her telangiectases did not begin until she was 30. At first a single naevus appeared on the right cheek, and in the course of years developed on the face, ears, and tongue, and finally on the hands at the age of 61. From the time the naevi appeared she suffered from 8 to 10 nose-bleedings a year, so severe that towels were soaked with the blood.

Sixteen years before admission she became breathless on walking uphill, and was admitted to a nursing-home, where iron-deficiency anaemia with achlorhydria was diagnosed. Iron was given, and she felt better until 1942, when breathlessness again occurred. In 1948 she had melaena, followed by loss of consciousness, and on being admitted to hospital 5 pints (2.8 litres) of blood was transfused. Subsequently folic acid and iron were given. She improved steadily, but had a severe bleeding from an angioma on the tongue in April, 1949; this ceased after cauterization, and a further 2 pints (1.14 litres) of blood was transfused. In February, 1950, her abdomen began to swell and her liver was enlarged. She was admitted with a provisional diagnosis of Osler–Weber–Rendu syndrome and cirrhosis of the liver.

On examination she was extremely pale; multiple angiomata were seen on the face, lips, and inside of the mouth, and scattered on the trunk; there was gross ascites, with enlargement of the liver and spleen (Figs. 1 and 2). Her blood pressure was 170/90. A haemic murmur was heard over the base of the praecordium.

Paracentesis was performed, and 7½ pints (4.3 litres) of clear amber fluid with a protein content of 1.2% and a lymphocytic cellular content was withdrawn.

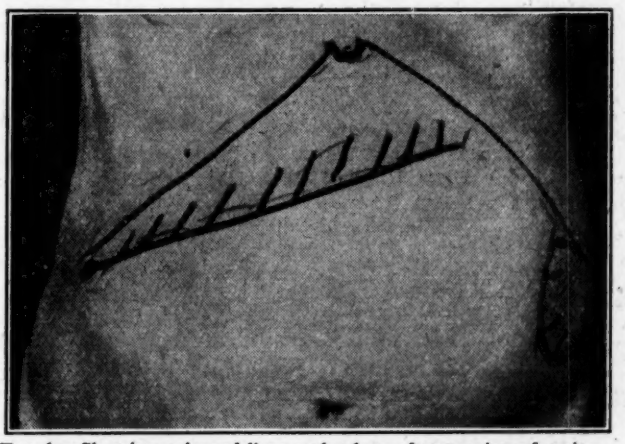

FIG. 1.—Showing enlarged liver and spleen after tapping of ascites.

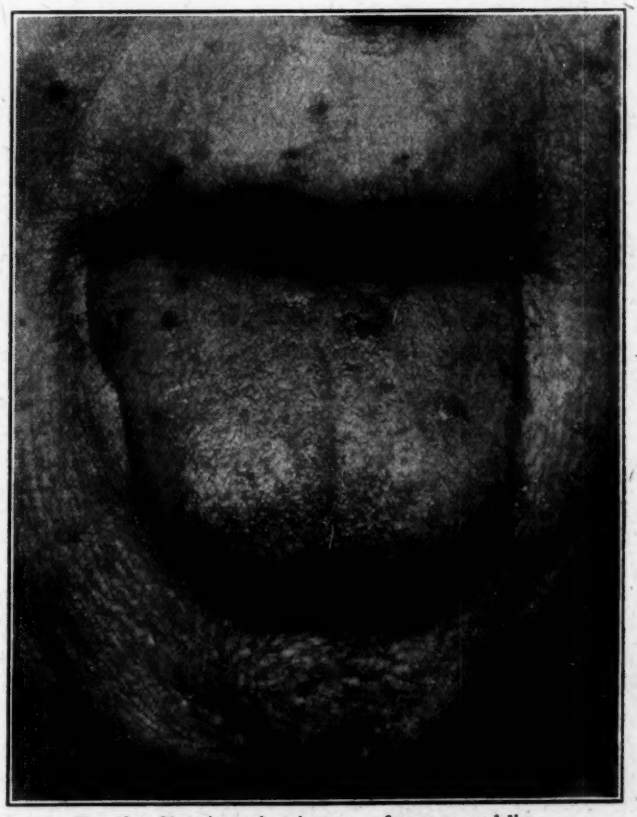

FIG. 2.—Showing telangiectases of tongue and lips.

A blood count showed: red cells, 2,450,000; haemoglobin, 42%; colour index, 0.86; white cells, 3,050; platelets, 346,000 per c.mm.; cell volume, 21.4%; M.C.V., 95.6 μ^3; M.C.H.C., 28%; bleeding time, six minutes; coagulation time, initial clotting five minutes; complete clotting, eight minutes. The sternal marrow film showed increased haemopoiesis with normoblastic erythropoiesis. There were some deformed iron-deficiency normoblasts.

Tests for occult blood in the stools were repeatedly positive. The fractional test meal demonstrated a histamine-fast achlorhydria and blood in the test specimens. The blood urea was 34 mg., and the plasma fibrinogen 250 mg. Liver-function tests on April 5 showed: serum albumin, 3.3 g.; serum globulin, 1.8 g.; serum total cholesterol, 190 mg. per 100 ml.; serum alkaline phosphatase, 20 units; van den Bergh, direct and indirect reaction negative; cephalin cholesterol, negative; thymol turbidity, 0.5 unit; colloidal gold, 33210. The serum albumin was relatively low, and the serum alkaline phosphatase was raised.

The patient's blood was found to be Rhesus-negative, and she was transfused with 3 pints (1.7 litres) of packed cells from Rhesus-negative blood. After this her red cell count rose to 3,390,000 per c.mm., and the haemoglobin to 60%. On April 28 she was discharged on choline, 4 g. a day, and "rutin," 60 mg. a day.

On June 8 she was readmitted. She felt better, but had had two further nose-bleeds and still had a pronounced pallor. The liver and spleen were unchanged in size. A blood count showed: red cells, 2,480,000 per c.mm.; haemoglobin, 36%; cell volume, 19.7 c.cm.; M.C.V., 79.4 μ^3; M.C.H.C., 25.4%; bleeding time, three minutes; coagulation time, initial clotting, eight minutes; complete clotting, 11 minutes; platelets, 275,000 per c.mm.; prothrombin time, 14 seconds. Tests for occult blood in stools were still strongly positive. Sigmoidoscopy failed to show any angiomata of the rectum and distal sigmoid colon; she was not submitted to gastroscopy. A further 3 pints of Rhesus-negative blood was given. She had no further nose-bleeds while in hospital, and was discharged on June 22.

On July 15 she was readmitted, the ascites having reaccumulated, but no further nose-bleeds having occurred. A blood count on July 16 was: red cells, 2,260,000; haemoglobin, 44%; colour index, 0.97; white cells, 4,050; platelets, 283,000 per c.mm. A further 12 pints (6.8 litres) of ascitic fluid was removed and she was discharged on July 17.

The patient's son, aged 33, had had angiomata of the cheek since he was 20. For five years he had had frequent nose-bleeds, up to three or four a week, and had required cauterization of the bleeding patches up to once a year. The daughter, aged 27, had had bleeding from both nostrils intermittently for 10 years, severe for seven years. There was one angioma on her left forefinger; this had only recently appeared. Neither had hepatosplenomegaly.

Comment

The above case illustrates the dictum that the true frequency of the condition would be realized if every physician, dermatologist, or rhinologist seeing cases of recurring epistaxis or multiple telangiectases of the face would inquire into the family history. The patient's daughter, although undergoing cauterization of the nose, was not previously considered to have hereditary haemorrhagic telangiectasia. All members of the family developed angiomata or nose bleeds after the age of 17. This is interesting, and recalls the work of Bean *et al.* (1949) on the angiomata of pregnancy, suggesting an endocrinological basis. The patient's severe anaemia was considered to be due to repeated blood loss in the stools, all tests for occult blood being repeatedly positive. Whether the bleeding arose from oesophageal varices as the result of cirrhosis of the liver, or from angiomata of the stomach or bowel, remains unproved, but Kushlan (1946) has described cherry angiomata and ecchymotic telangiectases, together with a distended oozing vein on the angulus observed through the gastroscope. The evidence for suspecting that the pathology is that of cirrhosis depends largely upon the presence of hepatosplenomegaly with ascites, the low value of serum albumin and raised serum alkaline phosphatase being of themselves inconclusive.

Treatment with rutin has been disappointing in this case, the anaemia relapsing within a few weeks of transfusion, and the nose-bleeds persisting despite doses of 60 mg. a day. This confirms the observation of Petch (1948).

Our grateful thanks are due to Dr. A. L. Peeney and Mr. Garfield Thomas for the pathological and biochemical work upon this case.

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AN INTERESTING CASE OF POLYMASTIA OBSERVED IN PREGNANCY

BY

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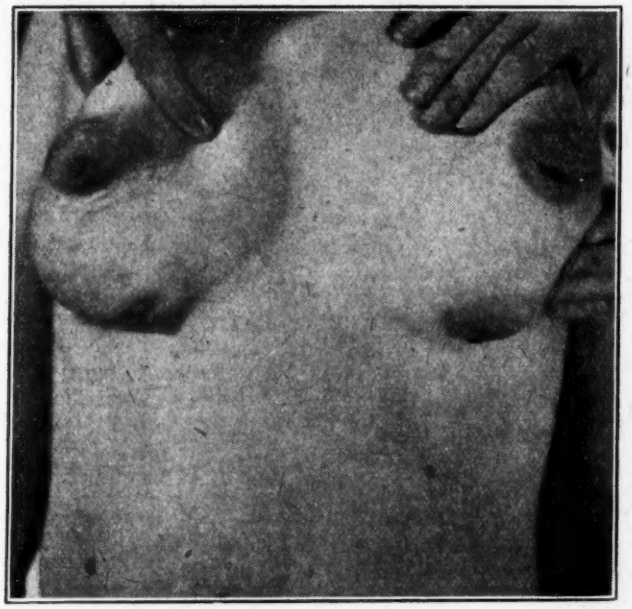
The occurrence of supernumerary nipples (polythelia) and of supernumerary breasts (polymastia) is well known. As students we meet first with these anomalies of development in the anatomy and embryology classes. In later days, in hospital or general practice, it is not uncommon to see patients in whom there are one or more supernumerary nipples; less frequently we may see a patient in whom supernumerary breasts are present. By the very nature of the examinations required, the hypertrophic and secretory changes which take place in the breasts, and the interest involved in breast-feeding, it is probable that most cases of polymastia are seen in pregnant women.

Case Report

A 2-gravida, aged 20, reported to the antenatal clinic of the Eastern District Hospital, Glasgow, on April 25, 1949. Her last menstrual period began on September 17, 1948, and her expected date of confinement was June 24, 1949. She had been pregnant on one occasion previously, and had delivered herself normally of a live male child weighing 6 lb. 8 oz. (2.9 kg.) in 1946. The baby was bottle-fed.

Her urine was clear of abnormal constituents, her blood pressure was 120/50 mm. Hg, and her weight was 9 st. 6 lb. (59.9 kg.). She made no complaint. She was of short

stature, and appeared otherwise normal and healthy. Examination of the chest revealed large breasts, which on closer inspection were seen to have bilateral secondary nipples and areolae on the lower curves, and in this region the breasts were locally slightly fuller. Colostrum could be expressed from each nipple. Lower down, on the abdomen, were two other supernumerary nipples. Arrangements were made, with the patient's consent, to record these findings by photography (see illustration). Examination of her heart



Photograph showing the extramammary glands with their nipples and areolae under the normal breasts. The supernumerary nipples on the abdominal wall are clearly visible.

and lungs did not reveal any departure from the normal. Abdominal palpation showed the uterus to be enlarged to a size consistent with a 26-weeks pregnancy: the foetal head was presenting. Her pelvis was examined and was considered to be of adequate proportions. The results of blood examination were: Wassermann reaction, negative; blood group, O; rhesus factor, positive.

From this time until she was admitted to hospital in labour she was seen regularly, and she remained well throughout the remainder of pregnancy.

She was admitted to hospital at 3 a.m. on June 24, her pains having started at 11 p.m. on the previous day, and a live female child weighing 6 lb. 9 oz. (3 kg.) was delivered spontaneously at 4.10 a.m. on the day of admission. The placenta (complete) and membranes (ragged) were delivered normally at 4.20 a.m.

It was decided to stimulate the milk secretion as much as possible, and when lactation was established the baby was to have test feeds from each of the four upper nipples. By June 27 the breasts were secreting very well, and it was considered that lactation was established adequately. Test-feeding was started on the following day. On the right side the baby did well from the upper normally placed nipple, but the secretion from the lower nipple was negligible, and test feeds on the right side were abandoned. On the left side comparative test feeds were satisfactory: from the upper normally placed nipple the baby was able to get an average of 14 oz. (400 ml.) of milk in 24 hours, and from the lower nipple an average of 7½ oz. (213 ml.) in 24 hours. The baby's weight-chart showed that it received adequate feeds. It was noted that from whatever nipple the baby was being fed the other three were stimulated to secrete spontaneously and freely. The patient co-operated very well, but it was obvious that she was suffering some discomfort by being almost bathed in milk at every feed, and, in spite of being screened, she felt embarrassed. Because of this it was decided to stop breast-feeding completely, and on July 2, the day of dismissal, she was given stilboestrol. Prior to dismissal her breasts were palpated and were found to be soft.

As a postscript to this case it is interesting to note that, according to the patient, her husband was unaware that his wife had the supernumerary breasts and nipples.

Discussion

References to abnormal development of the breasts are few, but one excellent account is that of Evans (1923).

According to *Gray's Anatomy* (1935), Hamilton *et al.* (1945), Evans (1923), and many others, there are fairly definite lines—the nipple lines, mammary or milk ridges—which extend on each side of the body ventrally from the roots of the arms to the inner aspects of the thighs in the groins. At any point along these lines it is possible for nipples and glands to develop by epithelial down growths. That this is so has been shown by Fisher (1947), who described a case of fibro-adenoma in breast tissue occurring in the groin. The normal breasts develop in the position which Evans (1923) states corresponds to the fourth archaic position, the first three of these positions being at a higher level. In the case described it is apparent that the normal breasts have appeared, and extramammary glands have developed in the fifth archaic position, that on the right being very rudimentary. In addition, at lower levels, supernumerary nipples have grown.

The mere presence of these anomalies of development is probably of little significance under normal conditions, unless on aesthetic grounds. During pregnancy and the puerperium, however, when the mammae are under the active influence of hormones, the importance of the extramammary glands may become evident, and in a negative way as in the case described. Because of the amount of milk which is secreted from all the glands when the baby is suckled at one, and the discomfort occasioned thereby to the mother, it may be necessary to stop breast-feeding. The position is paradoxical. It may be argued that the control of the secretion could be obtained by judicious administration of stilboestrol, but it is contended that the flow from the supernumerary breasts, though reduced, would continue, nevertheless, even though the extramammary glands were not suckled. The attitude of the mother, of course, must be taken into consideration also.

Summary

A case of polymastia in pregnancy is described in some detail, particularly with regard to lactation and breast-feeding.

In discussing the anomaly of development in the puerperium, it is held that breast-feeding is probably contra-indicated, the situation being paradoxical.

I wish to express my thanks to Dr. R. G. H. Cunningham, medical superintendent, for permission to publish the case report, to Dr. D. S. Anderson for the photography, to Mr. G. C. A. Terry, librarian, Royal Faculty of Physicians and Surgeons, Glasgow, for assistance with references, and in particular to the nursing staff in the maternity wards of the Eastern District Hospital, Glasgow, without whose capable assistance and co-operation the test feeding would not have been possible.

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Medical Memoranda

Torsion of a Tuberculous Pyosalpinx

Torsion of the Fallopian tube has been reported in this *Journal* by de Soldenhoff (1949) and Shaw (1949). It is a relatively rare condition, the total number of recorded cases since 1890 being about 120. In most cases the affected tube was diseased.

The following case of a twisted tuberculous pyosalpinx is worth recording because of its rarity and unusual clinical features.

Case Report

A nulliparous woman aged 21 was admitted to St. Giles's Hospital on August 14, 1949, complaining of dull lower abdominal pain of 48 hours' duration. The pain was of sudden onset and followed a short attack of diarrhoea, being at first general, and becoming localized in the R.I.F. some hours later. During the last 12 hours it had again become generalized, but remained maximal in the R.I.F. There was anorexia but no nausea or vomiting. Constipation followed the initial attack of diarrhoea. Flatus was passed a few hours before admission. During the last 24 hours scalding pain on micturition without frequency occurred. The gynaecological history, including the last menstrual period three weeks previously, was normal. Apart from occasional abdominal fullness after meals she had no previous abdominal trouble. During a routine examination in January, 1946, pulmonary tuberculosis was discovered. In May, 1946, a phrenic crush was performed. She was discharged after four months of sanatorium treatment and had remained symptom-free since.

Above: Torsion of tuberculous pyosalpinx, showing marked congestion and early gangrene. Below: Normal appendix from the same case.

On examination she was seen to be a well-built woman; facies slightly flushed; throat normal; tongue clean; temperature 100.6° F. (38.1° C.), pulse 124, respirations 22. Abdomen: normal appearance, soft, reflexes present; marked tenderness and guarding on deep pressure in R.I.F. and slightly in L.I.F.; positive Rovsing's sign and Cope's psoas test; shifting dullness in lower abdomen; a few borborygmi heard. P.R.: Very tender on right lateral rectal wall. P.V.: *Nil;* no palpable mass on bimanual palpation. Urine examination: Acetone ++, otherwise *nil*. E.S.R. 66. Blood count: red cells, 4,500,000; Hb, 72%; C.I., 80; white cells, 16,900 (normal differential count).

Acute appendicitis with pelvic peritonitis was diagnosed. Findings at operation (performed shortly after admission): A moderate amount of blood-stained fluid in peritoneal cavity; a dark plum-coloured, congested, mobile mass, the size and shape of a large pear, lying against lower caecum in R.I.F. (see photograph). Appendix normal. Mass proved to be right Fallopian tube, enormously dilated in its distal four-fifths. Most of the dilated portion had risen from the pelvis and, hanging over the pelvic brim, had become an abdominal organ. Both ovaries and uterus normal in appearance and position. No adhesions. The right tube had become twisted five times in a clockwise direction, at the junction of the normal and dilated portions, resulting in complete strangulation, early gangrene, and pelvic peritonitis. No improvement in colour noticed on correction of torsion. Salpingectomy performed. Abdomen closed without drainage.

Tube contained thick, green-yellow, odourless pus. The post-operative diagnosis was acute torsion of a tuberculous pyosalpinx. This was confirmed by pathological examination: (1) Löwenstein culture: tubercle bacilli present. (2) Section: Greatly enlarged and distended Fallopian tube. Contents resembled caseous material. Section of wall showed granulation tissue containing a few tubercle bacilli.

Recovery was uneventful. The patient was discharged on the twelfth post-operative day and has since remained well.

Comment

This case resembled acute appendicitis. Features suggestive of tubal torsion (Cope, 1940; Nixon, 1948) were missing—for example, simultaneous pain and vomiting, and a palpable mass. The characteristics of tuberculous salpingitis (Dible and Davie, 1945) were also absent—for example, signs of chronic salpingitis, tubal thickening, contraction, dense pelvic adhesions, caseation, and abscess formation.

The aetiology of the torsion is obscure. In the absence of adhesions it may have been started by the curious initial short attack of diarrhoea, leading to violent peristalsis, and aided by a long pedicle

I wish to thank Dr. W. Feldman, medical superintendent, St. Giles's Hospital, for permission to publish this case. I am grateful to Dr. E. Brand, pathologist, Park Hospital, for his report.

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A Second Attack of Poliomyelitis

Second attacks of poliomyelitis, though very uncommon, have been reported by Alves and Pugh (1947) and by Lipscomb (1947). Older literature in this respect was reviewed by Wilson (1940). Attention has also been drawn to the effect of exercise in precipitating paralysis in poliomyelitis (Russell, 1947).

The following case, in which the paralysis of the second attack was probably precipitated by violent exercise, seems worthy of publication.

Case Report

A recently qualified medical man aged 24, of distinctive athletic ability, had obtained a house appointment in a London teaching hospital. His past medical history included typhoid, blackwater fever, and chronic sinusitis.

First Attack.—In September, 1947, while still a medical student, he underwent an operation for diverticulum of the bladder. Ten days after the operation he complained of headache, with photophobia, and pain in the back. His

temperature was 101° F. (38.3° C.). He had moderate neck rigidity and a positive Kernig sign. The cerebrospinal fluid showed a pressure of 80 mm. water, three cells per c.mm., and 30 mg. of protein per 100 ml. He developed some weakness of the left triceps and left extensor carpi radialis, and of the left foot. He was seen by a neurologist, who regarded the condition as a mild case of poliomyelitis with every prospect of complete recovery. He did in fact make an excellent recovery, but admitted to some residual weakness in the left foot, sufficient to keep him out of first-class rugby.

Second Attack.—On January 13, 1950, he reported sick with profuse sweating, increasing pain in the lower right chest, and hiccup. There was no dyspnoea, cough, fever, or other symptom. Later his temperature rose to 100.4° F. (38° C.), and the hiccup caused considerable distress. The throat, lungs, and abdomen were normal except for some tenderness of the recti abdominis. The evening temperature was 99.8° F. (37.7° C.); the pulse and respirations were normal. The following morning his temperature was up to 102.4° F. (39.1° C.), but was normal by the evening, and remained so the day after, when the pain had almost gone but some hiccup and headache remained. The chest examination and differential white cell count were normal. On January 17 he was free from pain and his temperature had been normal for 48 hours. He felt very well, and was given permission to go. A diagnosis of Bornholm disease had been made.

Apparently he felt quite well until the evening of January 19, when, while engaged in a violent game of squash, he developed a severe headache and later vomited. The headache persisting, he took some "veganin" tablets and went to bed. Next day he went away for the week-end, although not feeling well, and joined a party at a cinema in the evening. He felt cold and shivery, but as it was a bitterly cold night little notice was taken of this. He admitted to having a headache and feeling not well. Afterwards at supper he appeared to enjoy his meal and was quite bright and cheerful. He took some veganin and a hot toddy and went to bed early.

It had been intended to allow him to sleep late, but, movements being heard in his room, he was visited by his host, who immediately realized that he was seriously ill, with marked meningitic symptoms—namely, severe headache, neck rigidity, positive Kernig sign, and left plantar response extensor. He was perfectly clear mentally; his conjunctivae were congested, and photophobia was intense. His temperature was 100.4° F. (38° C.), pulse 100. Occipital and trapezius muscles were tender, but there was no tenderness elsewhere, and he was otherwise normal.

Specialists were called in, and they diagnosed poliomyelitis. In consequence he was removed to hospital, where the diagnosis was confirmed by the physician-superintendent. While awaiting removal to hospital he began to vomit, and this persisted. On admission he was found to have marked photophobia, intense headache, stiffness of the back and neck muscles, and his knee-jerks were brisk and plantar responses extensor. His abdominal reflexes were absent. Kernig's sign was present, and there was muscle tenderness. By the afternoon of January 21 there was some weakness of the adductors of the thighs, and the knee-jerks, though present, were diminished in activity. In view of the diagnosis of poliomyelitis it was at this stage considered inadvisable to do a lumbar puncture.

On January 22 he was still complaining of severe headache, and vomited at intervals. While he was being prepared for lumbar puncture his condition worsened, and he resented movement. He complained of respiratory embarrassment, which was obvious, the movements of his diaphragm and intercostals being weak. He was immediately placed in a Both respirator, where his condition improved, and he appeared cheerful but somewhat apprehensive. He had a comparatively restless night, having failed to sleep, though hypnotics were administered, and he was rational and in comparatively good condition on January 23. His neck, back, and limbs were still hyperaesthetic; the headache persisted, but the vomiting had ceased. There was no interference with speech, but some difficulty in swallowing. Suddenly, without any warning, he became cyanosed; speech became difficult, and his condition critical. He died of cardiac and respiratory failure an hour later.

Sections of the spinal cord and brain were taken at necropsy, and the pathologist reported: "Sections from the lower cervical, thoracic, and lumbar regions show the characteristic changes of acute poliomyelitis. The grey matter shows much infiltration with inflammatory cells, including many polymorphonuclears; the motor nerve cells are necrotic; and the blood vessels show perivascular cuffing. The medulla also shows focal areas of inflammation and perivascular cuffing, but the pons and optic thalamus are normal."

Comment

On the evidence available this man had two attacks of poliomyelitis within just over two and a half years, the first being mild, from which almost full recovery was made, and the second a fulminating attack, which caused death. The second attack ran a typical course showing plainly the biphasic progress (McAlpine *et al.*, 1947) of the disease, there being an interval of two to three days between the illness of the invasion and the onset of the paralytic phase. During the remission he felt well enough to play such a strenuous game as squash. It is possible that had he remained quietly in bed during this remission the illness would have terminated as an abortive attack of poliomyelitis, without paralysis.

I am indebted to Dr. Douglas McAlpine for his suggestion that I should publish this case; to Dr. R. J. McGill, Dr. D. J. N. McNab, M.O.H., Christchurch, and Dr. George Chesney; and to the teaching hospital for supplying the patient's previous medical history and notes on the first phase of his second illness.

E. C. PARKER WILLIAMS, M.R.C.S., L.R.C.P., D.P.H.

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The latest issue of the *Bulletin of Animal Behaviour*, an occasional publication of the Association for the Study of Animal Behaviour (Cromwell House, Huntingdon), contains several interesting articles, including English translations of three recent papers by Professor K. von Frisch on the language of bees and on their orientation. As is now well known, bees communicate by dancing in certain significant patterns, and it has now been shown that they can perceive the plane of polarization of the light reflected from the sky—the plane changing as the sun changes its position through the day. In this way bees, and apparently ants also, can find their way about with reference to the sun's position even when the sun itself is obscured by cloud. The careful experiments described in the paper make these ideas, which at first seemed fantastic, completely credible and convincing. Another article, by Professor O. Koehler, discusses the ability of birds to count. He points out how careful one must be in animal experiments not to give away the right answers to test questions by some slight unconscious sign. The horse Clever Hans, for instance, which was at first thought to be capable of complex mathematics, was in actual fact only an adept at responding to the tension felt by his master as the correct answer was approached. In the latest work, however, ravens, parrots, jackdaws, and other birds have been shown able to count in the complete absence of human beings—when it was to their advantage to do so.

Reviews

PHYSICIAN AND HYGIENIST

A Biography of Sir Benjamin Ward Richardson. By Sir Arthur Salusbury MacNalty, K.C.B., M.A., M.D., F.R.C.P., F.R.C.S. (Pp. 92. 7s. 6d.) London: Harvey and Blythe, Ltd. (212, Shaftesbury Avenue, London, W.C.2). 1950.

"Richardson's energy and endurance were phenomenal. No subject in or near the sphere of medicine did he leave untouched; in many of them he showed some originality of conception: and none did he fail to enliven with some fresh illustration." So wrote Clifford Allbutt in a notice of this tireless and faithful lover of Hygeia. The period of scientific activity of Benjamin Ward Richardson (1828–96) covers almost exactly the second half of the nineteenth century, for his first paper, "On Fibrinous Elements of the Blood," appeared in 1851, while the two volumes of his valuable *Disciples of Aesculapius* were collected by his daughter and published posthumously in 1900. Versatile though he was and various though were his contributions, he was before all else a clinical physician and a hygienist. The *British Medical Journal's* symposium on "Fifty Years of Medicine (1900–1950)," recently published as a book, illustrates the first half-century of *scientific* clinical approach. Clinical medicine and hygiene have become sciences in that half-century. Before then there were plenty of scientific medical men, but the actual approach to clinical medicine and hygiene was still too traditional for these to be justly numbered among the sciences. Thus the second half of the nineteenth century may be regarded as a prelude to scientific medicine. In that prelude and in that great movement Richardson holds an honoured place.

Born in 1828, he lost his mother in 1838, and decided then to devote himself to medicine. At 16 he was apprenticed to a local apothecary in Leicestershire. Soon after he went to Glasgow for medical training. Salient events of his student life there were his presence at the first operation under a general anaesthetic at the Royal Infirmary in 1847 and his contraction of typhus and long convalescence therefrom. After working with several country practitioners he qualified as a licentiate of the Faculty of Physicians and Surgeons of Glasgow in 1850. He then became an assistant to a firm of general practitioners at Mortlake. Here he spent four busy, happy, and profitable years, and made several contributions to medical literature. In 1854 he settled in London as a physician. He did not attain first rank among London consultants and was not elected to one of the great teaching hospitals, the staffs of which were then, and long remained, very close corporations. He obtained, however, extensive clinical experience in a number of relatively minor hospitals, and he accumulated teaching experience in forensic medicine in a private medical school, in materia medica at the Royal College of Physicians, and in anatomy at the College of Dentists. He established a considerable reputation in legal medicine.

Throughout life the literary activity of Richardson was immense. In 1855 he founded, edited, and largely wrote the *Journal of Public Health and Sanitary Review*, which for some years incorporated the *Transactions of the Epidemiological Society*. In 1862 he founded the monthly *Social Science Review*. In 1884 he began the long series of original essays known as "The Asclepiad," which were continued till shortly before his death and are still often consulted In addition to these, he was responsible for nearly a score of independent volumes on subjects as varied as the treatment of phthisis (1857), coagulation of the blood (1858), relation of dental to general disease (1860), disease of modern life (1875), alcoholism (1875), manufacture of bread (1884), public health (1887), artificial respiration (1890), to say nothing of a novel which is of considerable merit.

Richardson was an excellent biographer, a learned historian, no mean experimenter, and an understanding and penetrating physician in the days when knowledge of human nature and intuitions about disease states were the main stock-in-trade of the physician. Above all he was a devotee of the hygienic idea. He was thus specially equipped to edit the work and write the life of Edwin Chadwick. This he did in the two fine volumes published in 1887 as *The Health of Nations*. This, with his *Disciples of Aesculapius*, published with an account of his own life by his daughter in 1900, are his most permanent memorials. He will, however, always be remembered as an able, eloquent, energetic, and, withal, sane advocate of temperance. In 1875 he became himself a total abstainer, but, in 1888, in a clinical study of the action of alcohol, he wrote: "Between the general use of alcohol as a supposed food, and its use as a medicinal agent, there is the broadest distinction. I have never given up the medicinal use of opium or alcohol."

"Call no man happy until he is dead; he is, at best, but fortunate," said Solon of Athens two and a half thousand years ago. This fine, manly, humane, inquiring being, B. W. Richardson, was fortunate in his life. But he is also happy in finding as memorialist one not unlike himself and not unworthy to be classed with him.

CHARLES SINGER.

HUMAN PHYSIOLOGY

Physiologie des Menschen (Landois-Rosemann). By Dr. Med. Hans-Ulrich Rosemann. Twenty-sixth edition. (Pp. 958; with 240 figures and one coloured plate. M. 46.60.) Berlin: Urban and Schwarzenberg. 1950.

The present editor of this famous work is the son of Rudolf Rosemann, who produced the eleventh to twenty-fourth editions of the book, which originated as the textbook by Landois published first in 1879. The scope of the work is wide, covering a good deal of biochemistry and of pathological and clinical physiology. It contains an enormous amount of information, which is accordingly somewhat tightly packed, and among other features has interesting paragraphs on the history of the subject. As the book has grown with the subject it has retained many traces of its evolution, and some of these could with advantage be omitted, since they now fall into the range of other subjects. As an example of this sort of thing one may perhaps mention a large amount of space given on p. 451 to the properties of drinking water; again, nearly a page is devoted to sputum on p. 225.

The emphases given are different from those in books in English. Thus *nor*-adrenaline is only lightly touched upon, and pancreozymin not mentioned. To make up for this we have innumerable examples of the German-speaking point of view and references to literature. These last would be more useful if the system of numbering was such that the reference could be located without

the reader having to turn back to find what number chapter he was reading. Could this perhaps be printed on each left-hand page heading?

C. LOVATT EVANS.

TEXTBOOK OF GYNAECOLOGY

A Textbook of Gynecology. By Arthur Hale Curtis, M.D., and John William Huffman, M.D. Sixth edition. (Pp. 799; 466 illustrations, chiefly by Tom Jones, including 37 in colour. £2 10s.) Philadelphia and London: W. B. Saunders Company. 1950.

When I first turned over the pages of the sixth edition of this textbook my admiration was profound. It is a beautiful production—good paper, superb illustrations, clear text, and attractive binding. Then I studied it more closely and admiration was at times intermingled with some concern, so much so that restful sleep became impossible that night. Why was it that something so very good could at times appear almost unfinished?—that was the question whose answer proved elusive. Then in the early morning hours there came the perfect quotation with which to begin the perfect review of such a book. It pointed out its faults without detracting from its inherent value. It was perhaps severe, but kindly none the less. If the book was not exactly a masterpiece there was no doubt that the review would be. With this assurance came peaceful sleep until the dawn. Unfortunately, with the rising of the sun the wording of the quotation could no longer be recalled, and the following must suffice as an unworthy counterpart.

The general arrangement of the book is good and the emphasis on clinical observation and accuracy is most refreshing. "Bedside visits should include inspection of the tongue and notation of the pulse. The modern tendency is to neglect this evidence. A dry tongue tells more than voluminous charts relevant to the patient's need for liquids." The page from which this is extracted could well be framed in gold, and extracts suitably chosen would make admirable Christmas presents for members of both the medical and the nursing staff responsible for post-operative care.

The main weakness of the book is illustrated by the sections on infertility and carcinoma of the cervix. They remind one of the inexperienced house-surgeon who has recorded with great care a detailed history of his patient, and the findings of a thorough examination, but at the end of it all has no concise picture of the particular clinical problem requiring solution. His mass of detail obscures the main issues. For example, the reader interested in infertility will find a full account of the subject, but the section would be more useful if there were a brief, summarized description of the sequence of investigations practised and advocated by the authors. Those for whom the textbook is primarily intended require clear guidance on these practical details. In the same way we read of carcinoma of the cervix that "when symptoms first appear we can cure nearly every cancer of the external cervix," and that "there is widespread confidence in the great value of high-voltage deep *x*-ray therapy in the treatment of cervical cancer." "The insertion of a radium bomb" is then advocated, with the dosage expressed in mg.-hours, but the authors do not refer to the help a physicist can give in making radiation therapy both effective and safe. General statements such as, "The male hormones are useful," and, "Resection of the presacral nerve should find a limited field of usefulness," leave the reader thinking of the words of a famous slogan, "Say when!" Such incompleteness is found in only a few places. If remedied in the next edition a good textbook will become an excellent one.

J. STALLWORTHY.

DIAGNOSTIC BACTERIOLOGY

Diagnostic Procedures and Reagents. Technics for the Laboratory Diagnosis and Control of the Communicable Diseases. Third edition. Edited by R. S. Muckenfuss, M.D. (Pp. 589; illustrated. $6.) New York: American Public Health Association. 1950.

This is a manual of laboratory methods approved by the American Public Health Association, in the compilation of which 30 authors have participated. Most of the chapters are on methods for cultivating and identifying particular bacteria, or otherwise diagnosing individual types of disease. This system of presenting the material leads to some repetition, and methods of obtaining and examining certain kinds of specimen are described repeatedly.

Most accounts are purely technical, but that of leptospirosis deals also with history, epidemiology, and other aspects of the subject. Some authors are content with describing a single recommended method, and others give the choice of several without always indicating their relative value: those suggested for determining virulence in *C. diphtheriae* include one employing chicks and the *in vitro* method of Elek. The chapter on syphilis is only a general essay on progress and policy in connexion with serological diagnosis. Other subjects are Rh testing, culture media, blood cultures, and "antimicrobial assays." The account of the last is disappointing, the only procedure suggested for determining sensitivity to antibiotics or for assaying them being a simple tube-dilution method. There is a good chapter on malaria, well illustrated, and the illustrations are also numerous and helpful in that on mycoses, which provides adequate technical instructions and keys to the identification of all the main species of pathogenic fungi.

The methods used in different laboratories vary so widely that everyone has something to learn from a book like this, even though in some instances he may prefer his own technique to that described.

L. P. GARROD.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

A Handbook of Ophthalmology. By H. Neame, F.R.C.S., and F. A. Williamson-Noble, F.R.C.S. 7th ed. (Pp. 338. 22s. 6d.) London: J. and A. Churchill. 1951.

Tropical Nutrition and Dietetics. By L. Nicholls, C.M.G., M.D., B.C., B.A. 3rd ed. (Pp. 476. 42s.) London: Baillière, Tindall and Cox. 1951.

The Law Relating to Mental Treatment and the Health Service. By H. Berry. (Pp 121 8s. 6d.) London: J and A. Churchill. 1951.

Textbook for Health Visitors. By L. Roberts, M D., M.R C P., D.P.H., and others. (Pp. 551. 21s.) London: Baillière, Tindall and Cox. 1951.

Infant Feeding and Feeding Difficulties. By P. R. Evans, M.D., M.Sc., F.R.C.P., and R. MacKeith, M.A., D.M., M.R.C.P., D.C.H. (Pp. 255. 12s. 6d.) London: J. and A. Churchill. 1951.

Antenatal and Postnatal Care. By F. J. Browne, M.D., D.Sc., F.R.C.S.Ed., F.R.C.O.G. 7th ed. (Pp. 703. 30s.) London: J. and A. Churchill. 1951.

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THE ENIGMA OF DISSEMINATED SCLEROSIS

The aetiology of disseminated sclerosis remains obscure, in spite of research which is being carried on all over the world. The view that the disease is infective is held by some,[1] but the clinical course is unlike that of any known infection of the nervous system: the pathological lesions differ from those in any proved infection due to a neurotropic virus, and there is only one suggestive report of experimental transmission of the disease. Margoulis and his associates[2] in Moscow isolated a virus from the blood of a patient with acute relapsing encephalo-myelitis and from the brain of a fatal case of acute disseminated encephalo-myelitis and reproduced the disease in experimental animals. They carried out neutralization tests with these viruses against sera from patients who had recovered from acute attacks of disseminated encephalo-myelitis, finding that the virus was neutralized in 70% of cases, and also against sera from 50 cases of chronic disseminated sclerosis, obtaining virus neutralization in 50% of these. There are apparently no confirmatory reports of this work, and there is grave doubt about the identity of acute disseminated encephalo-myelitis and acute disseminated sclerosis, though the history of the first Russian case is highly suggestive of the latter disease. Putnam and his colleagues[3-5] suggested that the primary lesion in disseminated sclerosis is thrombosis of small venules in the central nervous system with patches of demyelination around them, and he thought that the cause of the thromboses was an alteration in the coagulability of the blood. These views on the primary pathological change have not been generally accepted, and even if they were confirmed the reason for the change in blood coagulability remains undiscovered. Possibly the most hopeful line of research is the observation of demyelination in experimental animals,[6-8] brought about by the injection of homologous or heterologous brain extracts with adjuvants—a technique to which we referred last week.[9] But, as Hurst[10] has pointed out, demyelination is the reaction of the white matter of the nervous system to injuries short of those immediately lethal to the tissues, and there is still a wide gap between "allergic" demyelination and the assumption that human disseminated sclerosis is an allergic disease. In this number of the *Journal* Dr. C. E. Lumsden discusses the problems facing a pathologist investigating the demyelinating diseases. He suggests that two disease mechanisms may be concerned in the causation of disseminated sclerosis, a preparatory exogenous mechanism which damages the white matter, and an endogenous process which results in the liberation of a myelinolytic substance which diffuses slowly into the surrounding white matter, though at present the possible "triggers" which may set the intrinsic mechanism into action remain unknown.

Some recent reports have indicated that there may be a relationship between disseminated sclerosis and some disturbance of the metabolism of metals. Innes's[11 12] work on the demyelinating disease of lambs known as swayback demonstrated that the essential cause of this condition was a deficiency of copper in the pastures on which the ewes fed, or in some districts a disturbance in the utilization of copper. He found that swayback in lambs could be prevented by giving copper supplements to the ewes during pregnancy. Ritchie Russell and his colleagues[13] subsequently reported that of seven men who had been investigating the problems of swayback at Cambridge four had developed a neurological disease which had the clinical features of disseminated sclerosis. This led to further investigation[14] of copper metabolism in patients with the disease. Unfortunately these have not as yet helped to clarify the problem, since the blood–copper content was found to be within normal limits. Although the excretion of copper in the urine was in general lower than in normal controls, values similar to those in normal people were obtained after injection of B.A.L., which suggested that there was no lack of availability of copper in patients with disseminated sclerosis.

The possibility that the development of disseminated sclerosis might be associated with an excess of lead was put forward by Cone and his co-workers,[15] who found traces of this element in the cerebrospinal fluid of seven established cases of the disease, but others[16 17] found

1 McAlpine, D., *Brain*, 1946, **69**, 233.
2 *J. Neurol. Neurosurg. Psychiat.*, 1946, **9**, 63.
3 *J. Amer. med. Ass.*, 1931, **97**, 1491.
4 *New Engl. J. Med.*, 1933, **209**, 786.
5 *Arch. Neurol. Psychiat., Chicago*, 1947, **57**, 1.
6 Ferraro, A., ibid., 1946, **52**, 443.
7 Lumsden, C. E., *Brain*, 1949, **72**, 198.
8 —— ibid., 1949, **72**, 517.
9 Leading article in *British Medical Journal*, 1951, **1**, 1002.
10 *Brain*, 1944, **67**, 103.
11 *J. Neurol. Psychiat.*, 1939, **2**, 323.
12 *J. comp. Path.*, 1940, **53**, 1.
13 *Brain*, 1947, **70**, 50.
14 Mandelbrote, B. M., Stanier, M. W., Thompson, R. H. S., and Thruston, M. N., ibid., 1948, **71**, 212.
15 *Arch. Neurol. Psychiat., Chicago*, 1934, **31**, 236.
16 Rabinowitch, I. M., Dingwall, A., and Mackay, F. H., *J. biol. Chem.*, 1933, **103**, 707.
17 Boshes, B., *Arch. Neurol. Psychiat., Chicago*, 1935, **34**, 998.
18 *Brain*, 1950, **73**, 52.

the metal in the cerebrospinal fluid in only two out of twenty-seven cases in one series and in one out of sixteen in another. Campbell and his colleagues[18] have investigated the place of lead as an aetiological agent in a different way. During a survey of the distribution of the disease in rural districts they found one village where six people living within 500 yards of each other had developed the disease: they had all spent the first 20 years of their life in the village, although neurological symptoms did not develop in two of them until they had moved to other districts. In this village the soil had an abnormally high lead content compared with other places, though the reason for this was not apparent. In another village three cases of disseminated sclerosis occurred in cottages not far separated, and here also the lead content of the soil was unusually high. These workers also investigated the lead content of the teeth in patients with disseminated sclerosis and in normal controls and found that in general the absolute lead content and also the lead content relative to the weight of the tooth was significantly greater in the patients than in the controls. He suggested that excess lead might influence essential enzyme systems in some people and in this way cause demyelination in the nervous system. These studies are far from conclusive and need confirmation from other parts of the country. They do, however, suggest that further work on trace elements might yield valuable results in the study of the aetiology of neurological disease. The importance of potassium in the normal functioning of muscle is already realized, and it seems probable from the excellent results of vitamin B_{12} therapy in subacute combined degeneration that cobalt is a necessary element for the proper nutrition of the spinal cord.

PHYSIOLOGICAL EFFECTS OF CORTISONE AND A.C.T.H.

The notable therapeutic successes of cortisone and A.C.T.H., though mostly of a temporary nature, have tended to divert attention from the important physiological role which these hormones undoubtedly play in the normal individual. The recent summary by Sprague, Power, and Mason[1] is therefore welcome. They recall that most of, if not all, the tissues of the body are influenced by these hormones, and a remarkable number and variety of the body's metabolic activities are significantly affected by them. In a brief review of the physiological effects of cortisone and A.C.T.H. such as Sprague and his colleagues have written it is possible to refer only to the most outstanding results obtained. Mote[2] has undertaken a more detailed review of the same subject.

The metabolism of protein, fat, and carbohydrate has been shown to be partly under the control of the adrenal cortex, which secretes several steroid hormones. Though there is apparently a considerable overlap in their activities, it is convenient to subdivide these hormones into three groups, each characterized by the same major actions. The first consists of those corticoids containing oxygen attached to the 11th carbon atom of the parent steroid nucleus. Compounds E and F are in this category. In the second group are the corticoids without oxygen on the 11th carbon atom: these include desoxycortisone and desoxycorticosterone. The latter, however, is probably not produced by the adrenal but has been synthesized artificially.[3] The third group consists of those corticoids in which an atom of oxygen replaces the characteristic side chain present on the 17th carbon atom of corticosterone. The steroids of the first group greatly influence the metabolism of protein, carbohydrate, and fat, but have relatively slight effects upon the body's salt and water economy. On the other hand, those of the second group have little of the former influence but are about 50 times as active as the 11-oxysteroids on water and electrolyte metabolism. The steroids of the third group are mainly androgenic in action but also have an important anabolic effect in protein metabolism. Steroids of all three groups appear to be secreted by human adrenals under the stimulus of A.C.T.H., but the 11-oxysteroids usually predominate. Cortisone, however, by depressing the production of A.C.T.H. by the pituitary, diminishes the activity of the adrenal cortex and may cause it to atrophy. The physiological results of giving A.C.T.H. and cortisone are usually very similar, but differences due to the presence of significant quantities of the other types of steroid may become apparent in some cases, depending upon the reactivity of the adrenals treated with A.C.T.H.

In experimental animals A.C.T.H. and cortisone readily induce hyperglycaemia and glycosuria; but in man the doses are small in relation to the body weight, and evidence of impaired sugar tolerance is therefore usually slight and apparent in only about one-third of cases treated. Overdosage, however, often impairs carbohydrate tolerance, with a consequent rise in the fasting blood sugar and the appearance of glucose in the urine. Part at least of the glycosuria may be due to a lowered renal threshold. The effects of the

1 *J. Amer. med. Ass.*, 1950, **144**, 1341.
2 *The Physiological Basis for the Action of A.C.T.H. in Human Beings*, 1951. Published by the Armour Laboratories.
3 Steiger, M., and Reichstein, T., *Helv. chim. Acta*, 1937, **20**, 1164.

hormones are relatively short lasting, and return to normal occurs within a few days of termination of the hormone therapy. In a very few cases, especially those with a family history of diabetes, a more severe upset of carbohydrate metabolism may ensue with symptoms of frank diabetes; this, too, is usually only temporary. In diabetic patients, of course, the symptoms of the disease increase in severity while they are under treatment with these hormones.

Cortisone, compound F, and A.C.T.H. increase nitrogen excretion, especially when given in high doses, such as 200 mg. of cortisone daily. With a dose of 100 mg. the nitrogen loss is usually trivial. The appearance of cutaneous striae and the increased excretion of uric acid and creatine are probably also signs of increased protein breakdown and impaired resynthesis. During A.C.T.H. administration the inhibition of protein synthesis caused by the 11-oxysteroids may be partly neutralized by the opposite effects of the androgenic corticoids secreted under its influence. A commonly observed effect of these hormones on fat metabolism is a change in the distribution of adipose tissue, leading to the "moon-face" and the "buffalo hump." Ketonuria, another indication of disturbed fat combustion, is a rare occurrence.

Study of Addison's disease brought to light long ago the importance of the adrenal cortex in water and electrolyte metabolism. Although the corticoids lacking oxygen on C11 are the most active in this respect, the retention of sodium and water and the loss of potassium induced by cortisone show that the 11-oxysteroids are also not without influence. With therapeutic doses of A.C.T.H. or cortisone the electrolyte and water disturbance is usually slight, but deficiency of potassium in the blood may become serious if not anticipated, and in patients with congestive heart failure the sodium and water retention may aggravate the symptoms. Less well studied, but of great importance, is the action of the adrenal hormones and hence of A.C.T.H. on the other endocrine glands. The effects on the gonads, the thyroid, and the posterior pituitary are largely mutual, and present a wonderful example of the constant interplay between hormones and endocrine glands. But from the therapeutic standpoint the greatest interest now lies not in the physiological influences, already closely studied, but in the manner in which these hormones enable individual cells to continue to function normally in very adverse circumstances. As Mote remarks, "The major physiologic role of the adrenal cortex appears to be that of rendering the cells of the body generally more resistant to injury from a wide variety of causes and may allow the cells of the body to function in a relatively normal physiologic fashion in a grossly abnormal cellular environment." This is perhaps the most remarkable of the effects of these hormones and the most important challenge to the experimental biologist.

PREMENSTRUAL TENSION STATE

Many women experience a minor degree of discomfort premenstrually, but when symptoms are severe enough to interfere with their ordinary life the condition is called the premenstrual tension state, a name introduced by Frank[1] in 1931. The syndrome becomes increasingly apparent over the 7 to 10 days immediately before the period and abates suddenly with the onset of the menstrual flow. There may be a predominance of psychical symptoms, such as irritability, depression, insomnia, and emotional outbursts, but somatic symptoms, including lower abdominal fullness and discomfort and painful swelling of the breasts, are nearly always present. The aetiology of this disorder remains obscure. Frank ascribed it to hyperoestrinism associated perhaps with a high renal threshold for oestrogens, and he treated his patients with sedatives and low-dosage irradiation of the ovaries. Israel[2] did not agree with Frank's views and preferred progesterone therapy. Greenhill and Freed[3] attributed the symptoms to the influence of the ovarian hormones in causing a retention of sodium ions and an increase in extracellular fluid throughout the body, including the brain. Certainly the premenstrual gain in weight may be as much as 7 lb. (3.2 kg.), and increased appetite and thirst are common symptoms. These authors therefore recommended the restriction of salt and fluid and the daily administration of ammonium chloride (3 g. in divided doses) for the 10 days immediately preceding the period. A few years later Freed[4] reported on the use of androgens in this condition. In severe cases he gave 100–150 mg. of testosterone propionate in a course of injections spaced through each cycle, but in mild cases he found that the sublingual administration of 10 mg. of methyl testosterone daily throughout the cycle, or merely for the 10 days before the period, might suffice to alleviate symptoms.

Recently Morton[5] has investigated 29 cases of the premenstrual tension state by means of basal temperature recordings, endometrial biopsies, vaginal smears, and hormone assays. It has long been firmly believed that the symptoms occur in ovular cycles only, but Morton claims that his evidence shows that they may occur in anovular cycles too, and he concludes that the condition is associated with a premenstrual relative excess of oestrogen due to absent or deficient progesterone secretion. The urinary output and the excretion of sodium, potassium, and chlorides were found to be markedly diminished premenstrually. Therefore he also advised the use of diuretics and a salt-restricted

[1] *Arch. Neurol. Psychiat., Chicago*, 1931, **26**, 1053.
[2] *J. Amer. med. Ass.*, 1938, **110**, 1721.
[3] Ibid., 1941, **117**, 504.
[4] Ibid., 1945, **127**, 377.
[5] *Amer. J. Obstet. Gynec.*, 1950, **60**, 343.
[6] Brown, W. E., and Bradbury, J. T., ibid., 1947, **53**, 749.

diet, but his main line of treatment was the administration of chorionic gonadotropin, trusting in its luteotropic effect to increase progesterone production. However, there is reason to doubt whether this hormone has such an action in the human, and certainly it cannot be helpful in anovular cycles, because it does not induce ovulation or corpus luteum formation.[6] Morton also observed in 16 of his patients a premenstrual increase in carbohydrate tolerance. He accordingly attributed the symptoms of weakness, easy fatigue, increased appetite, and tremulousness to hypoglycaemia and advised a high-protein–low-carbohydrate diet with frequent meals to counter this. While success has attended several methods of treatment, many of them of such complexity as perhaps to distract the patient's attention from the symptoms, it should be borne in mind that the premenstrual tension state is most commonly seen in the emotionally unstable, and its onset is often related to marital strife, domestic upset, or continued frustration. The practitioner may well find that a diligent inquiry into the patient's background and the lending of a sympathetic ear to her worries and problems, together with appropriate advice and reassurance, provide the soundest basis for successful treatment.

BLOOD AND SURGERY

"Is your English blood, then, so precious?" an unimpressed French visitor is supposed to have asked Moynihan, in the face of his painstaking haemostasis.[1] Bleeding is still the surgeon's most serious problem, but since Moynihan's time it has become recognized in two forms: first, as a danger to life during operation, and secondly as a major inconvenience in the surgical manœuvres. The first has been countered by a sharper understanding of the value and technique of blood storage and transfusion, but the second remains as an additional difficulty in operations where large areas of skin are manipulated, in neurosurgery, and in many thoracic and E.N.T. operations. The responsibility has come to be laid on the anaesthetist to provide as avascular an operating field as possible, for which purpose chloroform and spinal analgesics enjoyed an undeserved popularity. The problem has recently been studied more logically, and the surgeon's demands satisfied by a closely controlled spinal block[2] or arteriotomy.[3] In this issue Dr. R. P. W. Shackleton records his impressions of a year's trial of methonium compounds for producing controlled hypotension. He made most use of pentamethonium iodide, but changed later to hexamethonium bromide, which he found more certain in its action. On the strength of his experience he increased the dose to 50 mg. for a healthy adult, which he found lowered the systolic blood pressure to the region of 70 mm. Hg. Shackleton observes that the drug was most effective with the patient in the foot-down position, which strengthens the assumption made by Paton[4] in a recent issue of the *Journal* that the fall in blood pressure results from a relaxation of venomotor tone. The immediate post-operative stage was managed with great care. If the pressure remained low at the end of the operation the patient was placed in the head-down position or given an injection of "methedrine"; his head was kept low on the journey to the ward and his bed raised with blocks at the foot until the blood pressure became stable.

Apart from the extra anxieties in the unsettling transition from operating table to bed—particularly while there is a shortage of skilled staff—the administration of methonium compounds to reduce bleeding has the risks of reducing the circulation in the brain and other organs to a dangerous level, and of leading to post-operative secondary haemorrhage. There would also appear to be the danger of thrombosis in older patients and of embolism following pressure on the calves in the foot-down position. Shackleton dismisses the obvious dangers of the technique as "mostly theoretical"; but it is for the individual anaesthetist to weigh these against his sense of duty for providing the surgeon with a comparatively bloodless field. The less experienced anaesthetist would certainly be advised simply to keep local bleeding moderately controlled by maintaining a clear airway and providing sufficient oxygen, and to resist the surgeon's demands for perfection.

TUBERCULOUS INFECTION OF LYMPH GLANDS

Many diseases, both slight and severe, affect the lymphatic system; yet at the present time there is far less known about it than about any comparable element of the body. Large and important-looking organs such as the spleen and tonsils can be totally removed without any apparent harmful effect; the function of the lymphocytes is a mystery compared with what is known of the erythrocytes and the polymorphonuclear leucocytes; and the one undeniable task performed by the lymphatics, the absorption of fats from the intestine, appears to have no connexion with what may be their purpose elsewhere. Considering how often the other circulating body fluids are examined and the invaluable information to be gained thereby, the fact that the lymph is hardly ever investigated in disease becomes a strange one. Technical difficulties, of course, account for much of this neglect; the dissection of the lymphatic channels is difficult and the procuring of a pure specimen of lymph from the peripheral circulation almost an impossibility. Yet it is possible, even probable, that in the lymphatic system lie hidden the solutions to some perplexing problems.

Elsewhere in this issue Mr. B. S. Jones gives an account of tuberculous lymphadenitis as seen in Nigeria. What must strike anyone working in Britain are the great differences in the picture of the disease here and in Nigeria: the much higher average age of the patients, the diffusion of the infection in most of the cases throughout several groups of glands, and the

[1] Bateman, D., *Berkeley Moynihan Surgeon*, 1940, London.
[2] *Anaesthesia*, 1948, **3**, 134.
[3] *J. Amer. med. Ass.*, 1946, **132**, 572.
[4] *British Medical Journal*, 1951, **1**, 773.

very rapid and massive infection seen in young children are all definite points of variation. In this country most of the tuberculous infections of lymph glands suggest a direct spread from some fairly obvious source of infection—from the tonsils and adenoids to the glands of the neck, from the lungs to the mediastinum, or from the bowel to the abdominal glands. But there are other cases, of course, in which an isolated gland suddenly becomes affected with no obvious direct track of infection leading to it. The most likely source of such an infection is the blood stream, and it is to this that Mr. Jones attributes most of the cases seen by him. He recognizes the point that such infections frequently lie dormant until another infection supervenes and stirs them into caseation and suppuration, or, as he puts it, "may pull the trigger." The frequency of suppuration in tuberculous glands of the neck, draining areas where pyogenic bacteria abound, is in marked contrast to the quiet course and eventual calcification of so many glands in the chest and abdomen, where the infection is more likely to remain single. It is difficult to avoid the "old established conception," quoted by Mr. Jones at[1] the beginning of his article, that the lymph glands may be infected either by direct spread along the lymphatics from a primary focus or from the blood stream. Most surgeons would agree that the former route is the more frequent in this country, and there seems little doubt that the latter is commoner among Nigerians. But we are still left without an answer to a crucial question: Is the reaction in the gland a defensive mechanism that is helping the body to resist an infection, or can it be compared to the slaughtering of a weak garrison by an invading force, frequently aided by allies?

PHRENIC STIMULATION OF BREATHING

Intermittent electric stimulation of the phrenic nerve is a harmless and simple method of artificial respiration. Careful study of the method is a recent development, though it has been practised sporadically for many years.[1-3] Sarnoff and his co-workers have shown that stimulation of one phrenic nerve adequately aerates both lungs, the lung on the unstimulated side being ventilated by movements of the mediastinum.[4] In adults spontaneous respiratory movements stop as soon as phrenic stimulation begins.[5] This inhibition is, partly at least, a reflex phenomenon, since it disappears after section of the vagus nerves in dogs.[6] In emergencies requiring immediate artificial respiration the stimulating electrode is applied to the skin of the neck over the motor point of the phrenic nerve. When it is necessary to continue electrophrenic respiration for days or weeks, as in bulbar poliomyelitis, the electrode is applied to the phrenic nerve itself through a small incision made under local analgesia. No harmful effects have resulted from such prolonged stimulation. Patients so treated are nursed more easily than they could be in an iron lung, and there are other advantages.[7] The apparatus consists of a robust and portable box, no more complex than similar machines used regularly by physiotherapists in most hospitals, though the details may perplex those unused to electrical terms.

This method of artificial respiration is immune from the risks of circulatory collapse and emphysematous distension of the lung which may result from methods of inflating the lung by air or oxygen under positive pressure.[8] Thus phrenic stimulation would be expected to have advantages over other methods used in resuscitation of the newborn, and in an article appearing in this issue Dr. K. W. Cross and Mr. P. W. Roberts describe the use of this technique in asphyxia neonatorum. They show that phrenic stimulation through the intact skin can inflate the lungs of stillborn babies, and the respiratory movements so produced may be life-saving. It is clear that this is a practical method of resuscitation in hospitals equipped with the apparatus. As with all methods, the maintenance of a clear airway is of the first importance. A larger, controlled series is now needed to define more fully the value of this method compared with other methods in the treatment of neonatal asphyxia. The present study cannot fail to arouse greater interest in the rather neglected study of neonatal respiratory physiology. Cross's observation that phrenic stimulation does not inhibit spontaneous respiratory movements in infants underlines the differences which exist between their respiratory mechanisms and those of adults.

1 Annotation in *British Medical Journal*, 1950, **1**, 426.
2 *New Engl. J. Med.*, 1950, **242**, 340.
3 Cross, K. W., *Proc. roy. Soc. Med.*, 1950, **43**, 445.
4 *J. thorac. Surg.*, 1950, **19**, 929.
5 Whittenberger, J. L., Sarnoff, S. J., and Hardenbergh, E., *J. clin. Invest.*, 1949, **18**, 124.
6 Sarnoff, S. J., Whittenberger, J. L., and Hardenbergh, E., *Amer. J. Physiol.*, 1948, **155**, 203.
7 Sarnoff, S. J., Maloney, J. V., Sarnoff, L. C., Ferris, B. G., and Whittenberger, J. L., *J. Amer. med. Ass.*, 1950, **143**, 1383.
8 Sarnoff, S. J., Maloney, J. V., and Whittenberger, J. L., *Ann. Surg.*, 1950, **132**, 921.

"GUILTY DOCTORS"

The Committee Stage of the Bill to impose direct charges on Health Service dentures and spectacles revealed the great anxiety caused by this measure on the Government benches. About thirty Labour members abstained from voting and another five went into the lobby against the Government. Though safeguards are included to ensure that hardship does not prevent the needy from obtaining these appliances, a measure of this kind is bound to be unpopular because of the flood of propaganda for the "free" Health Service to which the public has been subjected in the last three years. Now there is a danger that an attempt may be made to explain these charges on the grounds that the medical profession is responsible for having impelled the Government to impose them in order to keep running a service whose operation would be perfect but for the greed or ignorance of the doctors.

1 *The Times*, May 5.
2 *Hansard*, May 2.

The Minister for National Insurance, Dr. Edith Summerskill, is reported to have commented[1] recently on the "extraordinary, unquenchable thirst of the public for medicine," adding that bottles and jars in every cupboard in the country were costing thousands of pounds. According to this report she considered that "the guilty men were the doctors who, through ignorance or to please or impress a patient, prescribed expensive, branded proprietary drugs." Splenetic outbursts of this kind contribute more to the harmony of a political meeting than to the smooth running of the Health Service. There is already adequate machinery to check overprescribing in general practice, and there is no reason to suppose that the hospitals are treating the sick extravagantly. In any case the proportion of proprietary medicines prescribed under the pharmaceutical services is only about 16% (cost, about 44%) according to the latest figures of the Ministry of Health. Clearly there is no widespread prescribing of proprietary drugs in order to "please" patients, and if the occasional case of overprescribing occurs it is checked. Ignorance there no doubt is, for doctors would not claim to possess the omniscience that some politicians assume. Dr. Summerskill may find evidence of "guilt" in the desire of a doctor to please his patients. But a doctor who ceased to please them would have travelled far from the ideals in which he was trained and would come to resemble—what Dr. Summerskill perhaps had in mind—a governess presiding over a rather unruly nursery.

The debate on the new Bill[2] also gave Mr. Bevan an opportunity, if any were needed, to attribute to doctors chief responsibility for abuse of the Health Service—"I would say that it is in the manipulation of fee-paying beds by specialists in hospitals. There is more abuse from that than in any other part of the Health Service. . . ." There is no evidence that these beds are being misused in any way, but irresponsible attacks on the integrity of doctors are to be expected now from one who, when in office, did not hesitate to lend wild accusations a responsibility derived from his office.

A health service "free" to everyone has always been a more attractive proposition to set before the public than an expensive scheme that everyone must pay for, but each side needs equal emphasis if the Service is to be properly used. Since the Chancellor of the Exchequer referred to the new charges in the Budget speech, the rather disingenuous view has been canvassed by opponents of them that they are a threat to the foundations of the scheme of social security codified in the Beveridge report during the war and built up since then. But the main principle of the Health Service—and it is whole-heartedly supported by the medical profession—is that no financial or other barrier should prevent a sick person from getting the attention he needs. Increase of real earnings, abolition of chronic unemployment, and other means of sharing or properly utilizing the nation's resources—all important features of social security—contribute largely to that end. Some parts of the Health Service must, within that framework, be available free at the time because of their expense; other parts may need looking into if financial stability is to be kept commensurate with quality. Money is limited, and extravagance in any sphere, whether in prescribing, as is alleged, or elsewhere, is regarded with as much disfavour by the medical profession as by the Government, for it detracts from the value of the Health Service as a whole. But whatever abuses of the Service there may be stem largely from the misleading conception of it in propaganda, including such speeches as are referred to here, put out for political purposes.

FESTIVAL OF BRITAIN

The London South Bank exhibition was opened by the King on May 4 beneath a heavy grey sky which soon began to pour penetrating rain, a fine touch of British weather to grace the first day of a show of British life and achievement. No wonder the Meteorological Office's display, selling souvenir weather forecasts inside the Dome of Discovery, was surrounded by a small crowd. The Dome is filled with other marvels of physical science and of biology, including some tropical medicine, but the chief centre of medical interest is the Health Pavilion close to Waterloo Bridge. On May 4 this was unfortunately less complete than most of the exhibition, and still lacked some display panels and a good many captions. But there was enough there to learn the outline of developments in physiology, medicine, and surgery through some surprisingly frank and terrifying photographs, and to see the contributions of Edward Jenner, Florence Nightingale, and others to the public weal. It is a display on a good professional level but unfortunately seems to lack a central theme: it suffers from trying to cover too much, in too great a technical detail, and with an undue emphasis on pure science. It seems a pity, for instance, that Florence Nightingale's great work for the Army's health and indeed for public health in general has not received mention alongside the description of her influence on nursing, yet space has been found for Mackenzie's polygraph. It might have been wiser to concentrate on the great British achievements of public health, of nutrition, and of surgery since Lister introduced antisepsis, and to have omitted the explanations of elementary physiology and most of the panels on blood transfusion—which has nothing especially British in it. However, in spite of these criticisms it is well worth a visit.

The next session of the General Medical Council will open on Tuesday, May 22, at 10.30 a.m. (not 2 p.m. as is usual), when the President, Professor David Campbell, will take the chair and will deliver an address. It is expected that the Council will sit again at 10.30 a.m. on Wednesday, May 23, and will conclude its business on that day; and that the Medical Disciplinary Committee constituted under section 15 of the Medical Act, 1950, will sit on Thursday, May 24, at 10.30 a.m. to hear disciplinary cases.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

MINOR AILMENTS OF THE FEET—II

BY

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Hallux Valgus

Hallux valgus is a very common cause of disability in the feet. Except in certain congenital cases, when the deformity may affect the interphalangeal instead of

FIG. 5.—Extreme degree of hallux valgus. The splaying of the feet and the rotation of the great toe are well shown.

the metatarso-phalangeal joint, the condition is usually associated with and dependent upon a splaying of the anterior metatarsal region (Fig. 5*). This splay occurs chiefly at the first interdigital space, so that the first metatarsal becomes widely separated from the others (*metatarsus primus varus*); it constitutes the primary cause of the whole deformity. The deviation is sometimes congenital, but much more often it is acquired as a result of excessive forces falling on the metatarsal region such as occur when high-heeled shoes are worn. As the metatarsal deviates *away* from the mid-line of the foot, the toe itself, tethered at its base by tendons and ligaments, is pulled *towards* the midline, thus producing the prominence of the metarso-phalangeal joint.

As secondary effects the toe rotates so that the nail faces sideways, an exostosis with an overlying bursa forms over the mesial aspect of the metatarsal head, the structures on the lateral side of the joint contract, the sesamoids are displaced towards the interosseous space, and the second toe passes into a hammer deformity. Treatment may be sought for aesthetic reasons or because of disability. In early cases in young patients a good deal can be done by the use of corrective appliances. A suitably designed elastic accumulator worn along the inner border of the foot, a night sandal to which the toe is strapped in the corrected position, special corrective padding and strapping as used by the chiropodist, may all be of value, but more important is the correction of the splaying of the foot by metatarsal straps and footwear made with a particularly snug-fitting instep. High heels must be forbidden, but if the foot has already become "set" in the high-heel position the change to low heels should be brought about gradually.

For more advanced cases these measures are insufficient and operative treatment must be adopted. The nature of the various procedures is outside the scope of this article, but inflammation of the bursa (bunion) may need the practitioner's attention. Often this is traumatic (non-infective) in origin and will subside with rest, but at times it goes on to suppuration and may discharge spontaneously, though this is hindered by the thickness of the overlying skin. Sulphonamides and antibiotics will often arrest the infection in the early stages but the necessity for surgical drainage may still arise, especially if there is any indication of spread to the cellular tissues. After subsidence of the infection a fistula may remain which discharges a small amount of glairy fluid. Although destruction of the bursa by injecting caustics through the fistula has been tried it has proved unsatisfactory, and the best treatment is removal of the bursa together with the underlying exostosis, an operation that with the help of antibiotics can nowadays be undertaken without the risk of spreading infection to the soft tissues, the joint, or the bone. For advanced cases of hallux valgus, when operation is for some reason contraindicated, some relief may be obtained by the fitting of appropriate pads by a trained chiropodist.

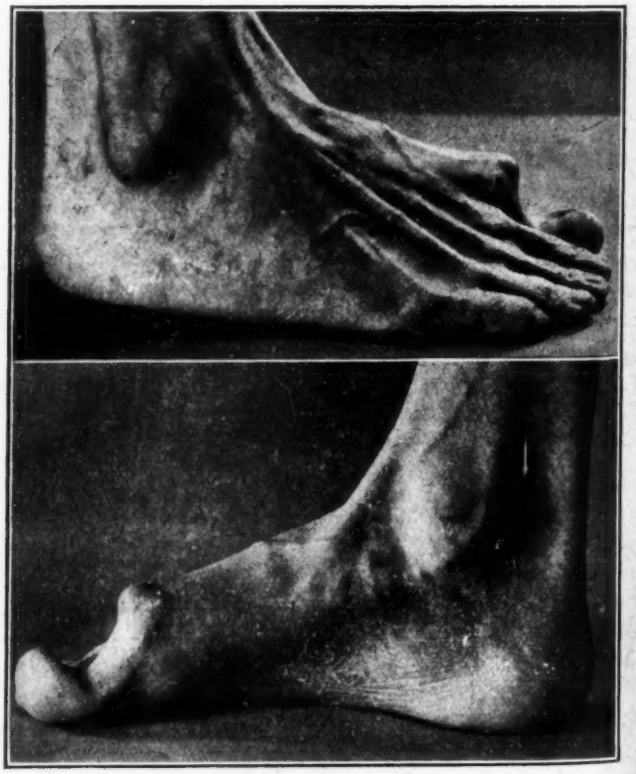

FIG. 6.—Extreme degree of hallux rigidus. This type is sometimes designated "hallux flexus."

*All the illustrations for this and the preceding article on "Minor Ailments of the Feet" have kindly been provided by the Photographic Department, Royal National Orthopaedic Hospital, London.

Hallux Rigidus

In hallux rigidus the causative pathology is an osteo-arthritis (probably of the wear-and-tear or traumatic variety) of the metatarso-phalangeal joint producing osteophytic ridges which mechanically limit the movements of dorsi and plantar flexion. The most troublesome cases are those in which the toe (often an unduly long one) is held rigidly in a position of plantar flexion (Fig. 6), for this interferes seriously with the "take-off." Patients adopt all sorts of dodges to overcome this difficulty in walking. The only treatment which can be expected to bring about a real improvement is surgical, but if this cannot be done a metatarsal bar must be fitted to the shoe.

A second type of hallux rigidus is seen in youth, in which there is no radiographic evidence of joint change. In these cases the rigidity is produced by muscle spasm secondary to a synovitis of the joint which may be traumatic or, as Trethowan suggested, toxic, arising from septic foci in tonsils or elsewhere. The treatment is that of synovitis locally and the clearing up of any focal sepsis. The injection of local analgesic into the joint relieves the spasm temporarily, occasionally permanently.

Hammer-toe

It has already been remarked that hammer-toe is often secondary to hallux valgus, but in some cases it seems to be congenital. If mild in degree it may be treated by suitable protective padding and by the use of a sandal to which the toe is strapped. In this deformity corns develop over the prominent interphalangeal joint and (in the so-called "mallet-toe") at the tip of the toe where it presses upon the ground. The former are prone to infection of the underlying bursa. In more severe cases surgical treatment is best; it consists essentially in excision of the interphalangeal joint so that bony union can occur between the phalanges in the straight position. This union is encouraged by the use of external or internal splints. Alternatively the "spike" operation may be done, in which the pointed end of the proximal phalanx fits into a corresponding depression in the cut end of the intermediate phalanx. The metatarso-phalangeal joint is not usually touched, though the deformity here constitutes an essential, and perhaps the primary, part of the whole deformity; however, the shortening of the toe which results from the excision relaxes the pull of the long tendons and so helps in the reduction of the dorsal subluxation at the metatarso-phalangeal joint.

Ingrowing Toe-nail

Ingrowth of the toe-nail (onychocryptosis) is, like many other foot conditions, usually attributed to the effect of tight or badly shaped shoes. The truth is that footwear is only a minor factor in its development. There are two distinct types of ingrowth of nails; the first is met with commonly in youths of 14 to 18, much less frequently in girls; the second occurs in later life and is often associated with an increased transverse curvature of the nails, especially with the "involuted" nail. In both types the great toe is the one chiefly involved. In the former variety the nail is fairly flat and wide, as is the toe itself, but it cannot be shown that the shoe has been exerting any undue pressure. It is prone to infection and suppuration in the lateral nail grooves, and this brings the patient for treatment.

Possibly the real cause is cutting the nail too short so that its termination receives no support from the pulp at the end of the toe when downward pressure occurs on the bony phalanx by the pull of the long flexor tendon during walking. The nail follows the phalanx and tends to bed itself in its soft surroundings, its lateral margins cutting their way into the rolled-over skin (Fig. 7). Once the nail is embedded the patient finds it difficult to trim the nail across right up to the edges and so a tongue of nail grows forwards on each side into the pulp: this is often called a "splinter." Careful removal of the whole

FIG. 7.—Advanced degree of onychocryptosis with inflammatory fungation in the lateral nail grooves.

of this splinter forms an important part of the treatment, for it will otherwise keep up the infection whatever other measures are adopted.

In slight and early cases, after the nail groove has thus been cleared and any granulations touched up with the silver stick or copper sulphate, a small piece of metal foil or gauze may be packed under the nail border and brought up over the prominent roll of skin. Sulphonamide and flavine powders help to overcome the infection. In persistent or recurrent cases I have no hesitation, however, in recommending amputation of the end of the toe, together with the whole of the nail and its bed, through the terminal phalanx, using a long plantar flap to cover the end. This operation gives a quick result, can be relied upon to be permanently successful, and causes no disability beyond the cosmetic effect of loss of the nail. Other surgical methods can be practised, but in my opinion they are less satisfactory.

In the other type of ingrowth the factors are different. Here it is the shape of the nail which is responsible for the ingrowth. With increasing age many toe-nails tend to become more curved, and shoe pressure, heredity, and vascular deficiencies all play their part in this change. In the involuted nail the lateral borders become rolled over upon themselves and are thus very difficult to trim. Pain arises from pressure effects, but actual suppuration is rare. A small corn or callosity develops on the rolled-over edge of skin and adds to the discomfort. In these cases operative measures are rarely necessary, but the lateral groove must be kept clear of all epithelial debris or hypertrophy, and the nail, which is usually unduly hard, must be trimmed with nail nippers. The occasional application of epithelial softeners, hydrogen

FIG. 8.—Onychogryphosis affecting all the nails, such as occurs in the aged and especially in bedridden patients.

peroxide or potassium hydroxide, to the groove is also of value. Some may prefer to have these troublesome nails dealt with by a qualified chiropodist.

Ram's Horn Nail

Onychogryphosis (ram's horn nail, Ostler's toe) is a less common condition which arises in two circumstances; in the first there has been a gross injury to the nail-bed, perhaps causing a subungual haematoma with separation of the nail; in the second, which occurs in the aged, the changes are probably brought about by vascular deficiencies in the nail-bed; it is often found in the bedridden (Fig. 8). A ram's horn nail is a nuisance because it precludes the wearing of ordinary shoes and is so hard that the patient is quite unable to trim it. It cannot be cured, for if the whole nail be removed the new one reproduces the deformity. In younger people the most satisfactory treatment is amputation through the terminal phalanx. In others the chiropodist may be able to reduce the nail to reasonable proportions by the use of his nippers and nail drills, often combined with some softening agent.

Plantar Warts

This infective papilloma of the sole of the foot is unique in that, owing to the thickness of the cornified layer of the overlying skin and to the pressures on the sole, it becomes pushed deeply into the tissues, leaving a flat smooth surface. For this reason it is often difficult to diagnose and resistant to treatment. Typically they are found in teenagers, especially girls, with a soft moist plantar skin, but they may be met with in later life. They are contagious and can be transferred from individual to individual, from one foot to the other, or to fresh areas on the same foot. The cause is almost certainly a virus infection; a portal of entry may be afforded by some small penetrating injury such as that produced by a nail in a shoe. The practitioner should suspect a verruca if he finds in a young person an apparent callosity in an unusual situation—for example, the hollow of the instep—which is very sensitive to the release of pressure, giving a throb of pain as the finger is removed. If some of the overlying callus be skived down the tips of the papillae may be observed, sometimes appearing as black spots if bleeding has occurred into them.

The very multiplicity of treatments advocated indicates that no entirely reliable one has yet been discovered. It would seem that on occasions a small verruca can disappear spontaneously, like warts elsewhere, and so add to the fame of the wart charmers. The chiropodist skives down the cornified tissue until the tips of the papillae are just exposed and then applies some caustic material—probably monochloracetic or trichloracetic acid, pyrogallic acid, nitric acid, and formaldehyde are the most popular. The process has to be repeated many times in the case of a large growth and is by no means painless. Carbon-dioxide snow can be used upon a small growth but is rather unreliable. Direct cauterization with a Paquelin or electric cautery, but better with diathermy, is a valuable method for surgical use. These warts extend surprisingly deeply and so thorough anaesthetization is essential if the whole growth is to be destroyed. This may be combined with curettage, but complete surgical excision is not recommended on account of the great tendency to recurrence in the scar. Radium (beta or gamma rays) and *x* rays are useful and painless treatments, but again the result is not always certain and it would be unwise to continue with such treatments for long.

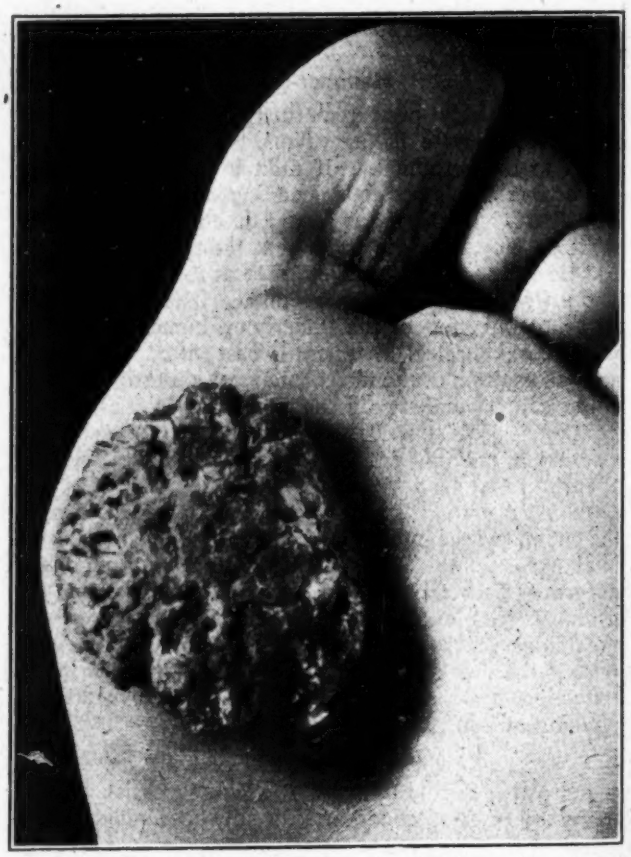

FIG. 9.—An extremely florid verruca showing the papillomatous structure of the growth. Usually, however, verrucae are buried beneath a thick layer of horny tissue.

In really difficult extensive and resistant cases (Fig. 9) I believe that thorough diathermic cauterization gives the best chance of cure. The wound left is a deep one, but not disproportionately painful, which will heal slowly under simple stimulant dressings. As the condition is very contagious it is necessary to institute common-sense prophylactic measures to prevent the spread of infection to others.

The very common fungus infections of the feet and nails have already been dealt with elsewhere in this series (see *British Medical Journal*, 1951, 1, 28).

REPORT ON THE WORK OF HEALTH VISITORS IN A CHILDREN'S DEPARTMENT IN HOSPITAL

BY

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In May, 1949, with the co-operation of the Cardiff City Health Authority, a scheme was started whereby two of the authority's health visitors were seconded to work in the children's department in United Cardiff Hospitals. This provided a practical link between the health authority and the hospital, the usefulness of which has become increasingly apparent as the experiment has proceeded. For some years it has been our custom to inform the superintendent health visitor for the City of Cardiff of the discharge of any child from hospital whose home we felt ought to be visited and whose mother seemed to need extra help and guidance. This was never a good arrangement, first, because of the inevitable delay in getting the relevant information to the district health visitor concerned, and, secondly, because the patient and his illness were relatively unknown quantities to her.

It seemed essential, therefore, that the health visitor should know these children while they were in hospital if she was to follow them up intelligently. Accordingly, two health visitors from the Cardiff City staff were seconded to work in the department of child health, and a report of their work for the year August, 1949, to July, 1950, is presented.

Health Visitors' Duties

The duties of these health visitors are divided between hospital attendances and home visiting. When in hospital they are present at the teaching rounds to undergraduates and generally take part in the work of the department by giving valuable information on medico-social histories of the children concerned. Thus, the medical student is introduced to the work of health visitors, and his interest stimulated in medico-social problems. During the child's hospital stay the health visitor learns his medical history and visits the child's home, bringing back useful and practical information. It is her practice to write a short account of her findings on the child's case notes. She thus makes herself known to the family and co-operates with them after the child's discharge. The child, too, knows her in hospital and welcomes an old friend. On the child's discharge from hospital the health visitor, armed with all the necessary medical information, sees that the medical aftercare is carried out, but as soon as she is satisfied that her attendance is no longer necessary the family are passed on to the health visitor of the district. Every encouragement is made to co-operate with the district health visitor and the home is visited together if possible. In order to strengthen further this link between hospital and public health department the hospital health visitors continue to share the accommodation with the other health visitors in their department in the public health offices. In addition, the hospital health visitors each have a small district of their own in which they act as routine health visitors.

The following list of duties summarizes the type of work done:

1. To pay an investigation visit to the home of the child while he is in hospital and to report on the suitability of the home and the parents to receive the child on his return, together with comments on the desirability of convalescence or special schooling, etc.
2. To supervise, on discharge home, the medical treatment ordered—for example, feeding, breathing exercises, medicines, etc., and, if need be, to contact the general practitioner in charge of the case.
3. To arrange for the child to attend the appropriate follow-up clinic, and if necessary to arrange for transport.
4. To advise and help in getting other members of the family or household medically examined—for example, for tuberculous contacts and familial disease.
5. To bring to the notice of parents the many organizations through which help can be obtained and guide them in their use—for example, National Assistance Board, Women's Voluntary Services, Order of St. John Medical Department, Queen's Nurses Association, Home Helps, Children's Officer, N.S.P.C.C., etc.
6. To give advice on when and how to obtain such benefits as free milk, vitamins, and school milk.
7. To report to the appropriate authorities any comments concerning housing or other social problems.

The Year's Work

Follow-up: August 1, 1949, to July 31, 1950

Children visited	361
Visits paid	2,935

Type of Cases Visited

Chest infection	143
Diarrhoea and vomiting	76
Nephritis and urinary infection	29
Miscellaneous	29
Feeding difficulties	19
Heart and rheumatism	17
Pyloric stenosis	16
Surgical	16
Convulsions	9
Anaemia and jaundice	7
	361

Case Reports

Two case reports illustrate the character of the work done:

Case 1.—A boy aged 12 years. In hospital with severe rheumatic carditis and heart failure. Discharged home on November 4, 1949. Home fairly satisfactory, mother a widow. Child to attend rheumatism clinic every two weeks. Ambulance conveyance arranged. November 14: walks around house a little. Front room being distempered by uncle, and child has bed downstairs. Mother informed she can get milk daily from school. January 10, 1950: name given for home teaching. January 19: readmitted to hospital. June 20: discharged from hospital; note sent to National Assistance Board for aid to buy single mattress, and note to St. John's about back-rest, bed-table, etc.; new chair supplied by W.V.S.; home teaching arranged; follow-up attendance arranged; supervision of doctor's treatment; nursing help given.

Case 2.—A girl aged 3 months. Admitted to hospital on March 16, 1950, with severe gastro-enteritis. Home conditions unsatisfactory—parents uncooperative. Local health visitor makes similar report. Reason for father's apparent hostility is that he has been out of work for 12 months awaiting hospital admission for hernia operation, and is embittered at having to be dependent on the National Assistance Board. Full particulars of financial position taken and National Assistance Board almoner informed. Advice given on sterilization of feeding utensils and general hygiene. April 29: baby discharged home. May 1: baby satisfactory, but house dirty and father hostile. May 5:

baby seen at infant welfare clinic; gaining weight but not taking vitamins. May 12: good progress—now taking vitamins; dirty bottle on table; further advice given on sterilization. May 26: financial grant from the National Assistance Board for clothing. June 4: free milk and vitamins obtained; baby well; transferred to district health visitor on September 17: father operated on in July, and later returned to work.

Comment

Criticism is sometimes heard that these arrangements may cut across and interfere with the work of the almoner. In fact, the almoner of the department works very closely with the health visitors and takes responsibility for carrying out many of the services that are recommended. This concord is made easier by their meeting at the bedside of the child as members of the department's staff. In practice we find that, whereas the health visitor's duties are primarily those related to the carrying out of medical treatment and those of the almoner the use of the social services available, the two have so much in common to contribute that there is manifest need for both.

It is our desire to establish a rota among the health visitors of the city for this hospital work. In this way postgraduate hospital experience will be gained by the health visitors in turn, and we believe their work will thereby be made more interesting.

It is hoped that this brief report of a year's work will be of interest to others who are anxious to wed the social and clinical sides of child health. To us it has been most helpful and stimulating to have the guidance and advice of these ladies in our department, and we believe that some such scheme should be introduced wherever local geography makes such an arrangement practicable.

HACKNEY HOSPITAL MATERNITY WING

On May 2 H.R.H. the DUCHESS OF GLOUCESTER formally opened a new maternity wing at Hackney Hospital and unveiled a commemorative tablet. The MINISTER OF HEALTH, speaking at the ceremony, said that no part of the National Health Service gave greater pleasure or pride than what was done for the treatment, care, and welfare of mothers and children. The decrease in infant and maternal mortality gave a feeling of satisfaction, but, although much progress had been made in this direction, the battle to save the lives of mothers and children must still go on. Hackney Hospital itself was a living example of the progress made during the last 100 years.

Alderman H. E. GOODRICH, chairman of the Hackney Group Hospital Management Committee, said that the new wing had accommodation for 109 mothers (including one bed for eclampsia cases). The original plan had been for only 86 beds, but, thanks to the enterprise of Dr. F. A. Bryning, the medical superintendent, it had been possible to extend the number and to introduce many other improvements which had not been thought of when the building was first planned in 1937. Her Royal Highness then formally declared open the maternity wing, and there followed a dedicatory prayer by the Bishop of Stepney.

The New Wing

Maternity beds are provided in wards of not more than six beds. There are observation windows in the doors of each bedroom, and patients can summon attention by means of light signals. In addition to the main ward lighting, each bed has its own wall-lamp, and cubicle curtains are installed in all wards having more than one bed. Each floor has a solarium provided with radiant heat, overlooking an ornamental garden. On the top floor is the receiving-room and four rooms, each with four beds, for antenatal cases; also an examination room, a doctors' room, and a comfortably furnished day room and balcony solarium. The delivery section is in the west wing of this floor. There are three first-stage rooms, two single and one three-bedded; four labour wards with Chassar Moir beds (one room larger than the others for operative delivery), and an operating room. The labour rooms, theatre, and the room for eclampsia cases have piped oxygen. There is a night nursery which can be used for babies who disturb their mothers' sleep. The premature babies' unit consists of a main nursery with thermostatically controlled heating and a "cooling-off" room, also with piped oxygen supply, and there is a special milk kitchen. Ultimately it is intended that one floor shall form an isolation floor. At present the ground floor is devoted to complicated cases, such as those requiring caesarean section. The baths are so designed that the nurse can have her feet under the bath and thus be directly above the patient for convenient lifting.

The Duchess of Gloucester was taken on a tour of the new department, and presented an inscribed silver christening cup to the first child to be born there. It may be added that Hackney Hospital is the responsibility of the North-east Metropolitan Regional Hospital Board, but the planning and the beginning of the execution took place while it was still under the London County Council.

CHIROPODISTS IN CONFERENCE

SIR HENRY COHEN ON PROFESSIONAL STANDARDS

Sir HENRY COHEN opened the annual convention of the Society of Chiropodists, held in London from April 26 to 28. He recalled the fact that it was the British Medical Association which initiated the movement leading in 1936 to the setting up of an independent Board of Registration of Medical Auxiliaries, and no organization had given the Board a fuller measure of support than the Society of Chiropodists.

"I have long been convinced," said Sir Henry Cohen, "of the major contribution which your work makes to the comfort and efficiency of mankind, and for 20 years I have been a Fellow of your society, not, I confess, having entered by the hard way." He went on to suggest that in place of the society's motto, *Post curam otium*, which was, after all, equally applicable to all forms of treatment, they should adopt the phrase used by Plutarch in telling how Pythagoras deduced the stature of Hercules from the length of his foot—*Ex pede, Herculem*—for this succinctly conveyed that aspect of chiropody which established its true status and purpose. The work of chiropodists was concerned with the foot not only as the site but as the index of disease. Those who had laid the foundations of the training of chiropodists had stressed the importance of bringing to the study a mind suitably prepared, and had demanded that appropriate standards in general education be attained. They had emphasized that modern concepts of disease and therapeutic measures depended for their understanding on the basic sciences of physics, chemistry, and biology; that it was necessary to know the normal structure and functions of the body if those disturbances, which were called disease, were to be recognized, and that before a disease could be prevented or cured its causes and effects must be known.

"Thus a syllabus has been devised which conforms to well-established and well-tried educational principles, and those of you who have had the advantage of being trained on the lines it lays down have been so well grounded in the understanding of your professional work that not only should you be competent to deal with the common problems of your craft but you should be able also to manage the unusual, the novel, and the unpremeditated situation, and—perhaps even more important—you will recognize that some of these problems lie outside the field of your own professional competence and you will seek aid from your professional colleagues. And you should not hesitate to acknowledge your limitations."

Medical Auxiliaries

In a reference to the Cope Committee on Auxiliary Services, Sir Henry Cohen said that there had been some resentment at the phrase "medical auxiliaries," and if it was used to imply a subordinate, an underling, a slave, to whom was assigned the drudgery and menial tasks of medical and surgical practice it was not difficult to understand the hurt. But chiropodists had achieved their professional status by accepting a course of training which gave them special knowledge and skills, and banded themselves together as a corporate body with 4,000 members and 500 students in training. The work of this body had been fully justified by the conclusions of the Cope Committee's report. But he reminded them that a profession had responsibilities as well as privileges. "You must always give of your best; you must not sacrifice yourselves to the worship of Mammon; you must maintain the highest ethical standards of practice; you must remain perpetual students of your subject so that those who entrust themselves to your care may feel confidence in your knowledge, your wisdom, your judgment, and your skill."

Lord AMULREE followed with an address in which he spoke of the medical care of the aged. He stressed the importance of keeping old people so far as possible mobile. The report on this subject by Dr. J. H. Sheldon in Wolverhampton had stated that 40% of the old people visited in the course of the inquiry were found to be suffering from foot trouble; these disorders were specially common among the women. A large number of old people, said Lord Amulree, would obviously benefit from chiropody services, and the absence of such skilled treatment was responsible for immobilizing them to a very great extent. A regular service of chiropody would relieve the hospitals of a considerable burden. He also mentioned the desirability of encouraging shoe manufacturers to issue a much greater variety of shapes and sizes. There would be far less need for chiropody if better-fitting shoes were available.

The programme of the Convention, over which Mr. JOHN H. HANBY presided, included visits to Guy's Hospital Annexe, Orpington, to see operations on orthopaedic cases, and to the Hospital for Sick Children, Great Ormond Street, to see operative and post-operative treatment for children. Mr. T. T. STAMM lectured to the members on the indications for, and the technique of, some orthopaedic operations, and other lectures were given by fellows and members of the society on various chiropodial techniques.

Preparations and Appliances

AN AID TO STARTING AND MAINTAINING DIFFICULT TRANSFUSIONS

Dr. C. A. McC. AITKEN, of Wembley, Middlesex, writes: For difficult transfusions I have found the following modification extremely useful and time-saving and quite as simple as the usual technique.

The needle with adaptor of the transfusion set is put aside and instead a fresh needle is used, attached through a small adaptor and tap to a 5-ml. syringe (preferably with

eccentric nozzle) half-full of normal saline. The needle should be of as wide a bore as possible. The 18 S.W.G. needle 1 to 1½ in. (2.5 to 3.75 cm.) long is of the same bore as the usual transfusion needle (1.25 mm.) and is obtainable from instrument manufacturers. Otherwise the 20 S.W.G. ordinary serum needle (bore 0.9 mm.) of the same length is quite useful, especially if the veins are small, though the tendency for slow running and stopping is greater.

This combination forms an efficient seeker for difficult veins, suction being applied to the syringe till blood flows. A small volume of saline is then forced through the needle to prevent clotting there. With the tap closed the syringe is replaced by the giving end of the transfusion set and the blood allowed to flow.

The syringe is kept in a sterile bowl and is always available for subsequent washing out of the needle, should this become blocked. The combination also greatly facilitates reinsertion of the needle into the vein. The process of restarting a transfusion is thereby greatly simplified and can be completed in a few minutes without any fresh equipment.

Reports of Societies

CONGENITAL PYLORIC STENOSIS

The Section of Paediatrics of the Royal Society of Medicine met on April 27 to discuss the "Treatment of Infantile Hypertrophic Pyloric Stenosis." Although the General Surgeons' and the General Practitioners' Sections had also been invited it was easy to spot the paediatricians. They were, on the whole, kindly-looking men; the younger ones (the Bloomsbury Set in the main) had the worried air of men who think largely in terms of electrolyte balances, and when they were seated one could see that they had not yet acquired the *savoir-faire* of their elder colleagues, who are ready to jump at the first sign of hydrostatic activity on the part of the baby. The meeting was very well attended, in part because it was 10 years since the subject had last been discussed, but also no doubt because the audience looked forward to a renewal of the controversy between physicians and surgeons. This, indeed, followed the expected lines, each side carrying its banner, in its own opinion, to victory, while a few cowardly onlookers preferred to have a foot in each camp.

Dr. KENNETH H. TALLERMAN briefly introduced the matter and then betook himself from the presidential chair to the rostrum as the first opener. He explained that until 1944 he had believed in the surgical treatment of this condition, but had then weaned himself successfully from such an impious belief. While admitting that in the last 15 years or so the surgical mortality had fallen from around 15% to 1 or 2% in expert hands, he was of the opinion that up and down the country it was most probably in the region of 15%. He was sure that medical treatment could do better than this. He accepted that the mortality of surgical treatment depended a great deal on whether the infant was breast-fed or artificially fed. (He quoted Levi's figures of no deaths in 100 breast-fed infants but a mortality of 11% in 46 artificially fed infants.) Since 1945 all his own cases had initially been treated with atropine methonitrate ("eumydrin"). He used a 0.6% alcoholic solution, and he stressed that the dosage must be adequate (15 to 25 drops per day). (This shocked Mr. Denis Browne into referring to babies "tottering on a heavy dose of a dangerous drug.") If after 72 hours vomiting persisted or the child failed to gain weight, he advised surgery. Of his own 67 cases in the last five years, 41 had had purely medical treatment and 26 had required operation. Since it was in any case highly advisable to spend two or three days in the preoperative preparation of a baby, by means of gastric lavage, the modification of its feeding regime and in administering subcutaneous saline, why, he asked, did not the surgeons allow the child the benefits of eumydrin during this period?

The Surgeon's Point of View

Mr. DENIS J. BROWNE accepted the president's challenge to fire a heavy barrage at the physicians. Commenting on Dr. Tallerman's assertion that the surgical mortality was

higher than the medical, he confessed that he was puzzled why, if all "failed eumydrin" cases could be passed on for operation, there was ever any medical mortality at all. He reviewed 600 cases treated by operation at Great Ormond Street during the war under conditions difficult for all parties concerned. The overall mortality had been 2%: that due to the operation itself *nil*. Mr. Browne explained in detail his technique, which he regarded as of very great importance. Local analgesia was essential; so was a high incision over the liver. He himself divided the rectus vertically, and he had devised a special weapon for separating the hypertropnied muscle of the pylorus.

Mr. DAVID LEVI differed from other surgeons in regarding congenital pyloric stenosis as an urgent surgical emergency. No time should be spent in "pre-operative preparation," and the only necessity was a stomach washout immediately before operation. He, too, regarded a local analgesic as essential, though he used far less of it than Mr. Browne. The operating theatre should be kept at 80° F. (62.2° C.). He disliked intravenous therapy or indeed fluids given in any way except by the mouth. He was powerful in his advocacy of breast-feeding. He was equally persuasive about the necessity for specially designed wards for children. The facilities he demanded brought to mind a cross between the Ideal Home Exhibition and Utopia —or, at least, the U.S.A. When he proceeded to outline the *minima* in respect of nursing staff, ward maids, etc., together with the precautions necessary to safeguard the health of babies in hospital, your reporter wondered whether he was listening to something from *Brave New World*, so aseptic did it all sound. It is of course true, as Mr. Levi said, that "ill babies will succumb to thoughtless action in hospital which a normal child will survive with impunity at home," but in these austere days it all sounded rather impracticable. Finally, Mr. Levi showed a really beautiful colour film of Rammstedt's operation.

Selective Treatment

The last of the opening speakers was Dr. NORMAN M. JACOBY, who described himself (presumably because he has the sense to live in the Weald of Kent) as a country bumpkin. He believed in "selective" treatment—that it should be possible to recognize clinically those cases which would respond to atropine methonitrate and those which would certainly require surgical treatment. His own cases were divided roughly equally and the decision was made when they were first seen. Since he did not think it proper for a physician to tell a surgeon what to do and when, he resolved the difficulty in a quite satisfactory, though somewhat Gilbertian, fashion: he did the job himself. He did not find it necessary either to give parenteral fluids or to wash out the stomach.

Dr. GEORGE DAVISON said that, although the disease probably occurred once in every 250 live births, this still meant that a general practitioner might see only one case every five or six years. It was therefore futile to expect him to know the finer points in diagnosis. What was important was that when a baby was vomiting without apparent reason a second opinion should be sought. And, further, that to lower the mortality cases should be referred to experts for treatment. But surely the fact that the "classical" picture of extreme dehydration was now so seldom seen indicated that practitioners were recognizing the cases early. He reported on a great number of cases from Newcastle-upon-Tyne. Between 1926 and 1950 1,100 had been seen. While stating that the mortality of the first 200 cases had been 15% and of the last 500 cases 3%, he took pains to point to the fallacy of figures. Dr. RICHARD DOBBS, on the same tack, showed some curves indicating that the improved mortality rate in pyloric stenosis followed almost exactly the curve of the infant mortality from all causes.

Mr. R. B. ZACHARY said it was all very well to give the credit for the present low mortality to breast-feeding, local analgesia, and fluids by the mouth, but when he was in Boston, Massachusetts, it was extremely rare to find a breast-fed baby, a general anaesthetic was always given (usually by a nurse), and it was unusual for a baby to escape without having something put into a vein. He was surprised that several speakers had said that medically treated babies spent no longer in hospital than those treated by operation. Most of the ones he operated on were home in three or four days.

A plaintive voice asked if anyone could tell him how eumydrin worked, and, though a large number of people must also have wished to know, no one was bold enough to speculate. In winding up the meeting, the president said it must be conceded that the treatment was still a controversial matter and that no doubt the physicians and surgeons would in general continue to differ in their beliefs. Although biased, your reviewer feels bound to record that he thinks Surgery won on points.

DISEASES OF THE RECTUM

At a crowded meeting of the Devon and Exeter Medico-Chirurgical Society, held on April 19, Mr. LAWRENCE ABEL spoke of some common diseases of the rectum and anal canal. Despite its name, he said, the rectum was not a straight tube, a fact to be borne in mind when dealing with, among other things, an imperforate anus.

How to Examine the Rectum

Apart from the skin no regions of the body were easier to examine than the mouth and rectum; nevertheless, more than half the cases of carcinoma in those regions came to operation too late to give the patient the best chance of cure. For efficient rectal examination four things were necessary: a couch, a good light, a rubber glove, and a non-greasy lubricant. The patient should lie, not in the Sims position, but on his right side, and the examination should be made with the left index finger. By this method a high neoplasm was less likely to be missed. The examining finger should be rotated through an angle of 360°. Confirmatory examination with a rectal speculum should follow, and if there was still doubt the lower bowel should be washed out and a sigmoidoscope passed. A barium enema, invaluable for the diagnosis of growths of the pelvic colon, could be fallible in the diagnosis of rectal growths.

Pruritus Ani

Mr. Abel touched upon the pathogenesis of first, second, and third degree haemorrhoids—spasm leading to congestion and ending in fibrosis; on their appropriate treatment; and on that of anal fissure and ischio-rectal abscess. Pruritus ani, once diabetes mellitus and threadworms had been excluded, might be due to lack of cleanliness or to roughly patched underpants. The condition should be treated by the establishment of a regular and normal bowel action, the intra-anal use of ung. hydrarg. subchlor. with cinchocaine hydrochloride ("nupercaine") suppositories, local painting with 20% carbolic, and, on the surface, an ointment of pulv. zinc. oxid. and lin. camph. with or without cinchocaine hydrochloride and made up with white petroleum jelly.

It should be remembered that simple neoplasms occurred in the rectum; pedunculated rectal polyps in children were easily and safely treated by ligating the stalk twice at a few few days' interval. Haematomata ani, also easily remediable, must not be confused with prolapsed haemorrhoids.

Mr. Abel ended by showing a film of the modern technique of abdomino-perineal resection for carcinoma of the rectum, the results of which were now highly encouraging. Nevertheless, because so many of these cases came too late to the surgeon 5,500 persons died annually of this disease. The presence of extensive metastases was not necessarily a contraindication to operation, for, with the primary growth efficiently removed, the patient could enjoy many years of comfortable and useful life.

Correspondence

Hospitality for Overseas Visitors

SIR,—May I once again appeal to members through your columns for offers of hospitality for our overseas medical visitors from the Dominions and Colonies?

As a result of a similar appeal last year (*Journal*, May 6, 1950, p. 1075) we received offers which were sufficient to cover our needs, and the visits which took place were much appreciated by our overseas friends. This year we expect a goodly number of overseas medical visitors, and there will be many among them who will much appreciate the opportunity of meeting us in our homes and so getting to know us better.

I shall be very glad if doctors willing to offer hospitality to an overseas visitor for one or two days, or even longer, would write to me stating what they are able to offer.—I am, etc.,

Empire Medical Advisory Bureau,
B.M.A. House,
Tavistock Square,
London, W.C.1.

H. A. SANDIFORD.

Unexpected Failure of Hexamethonium Explained

SIR,—Some time ago (December 30, 1950, p. 1496) I referred to a case of hypertension in a young girl of 16 (blood pressure 240/140) who failed to respond to quite massive doses of hexamethonium bromide by intramuscular and oral routes. This patient was submitted to operation for sympathectomy with the proviso that the left kidney be explored first, in view of the mild dilatation of the left renal pelvis visible in the pyelograms. This dilatation was minimal and thought to be of no significance by two urologists. It appeared to be caused by the pressure of what radiologically seemed to be a calcified lymph gland lying near the left renal pelvis.

Operation revealed a calcified aneurysm of the left renal artery, whose lumen in consequence was extremely narrowed. The kidney was not scarred nor apparently atrophic. Nephrectomy alone was carried out with an almost immediate drop in blood pressure. The patient has been up and about for several weeks now and the blood pressure still remains at this lower figure of about 135/80 mm. Hg.

This case appears to be a typical example of humoral hypertension due to renal ischaemia relieved by unilateral nephrectomy. The reason why it did not respond to hexamethonium bromide now becomes understandable if one postulates that the cause of the hypertension was not mediated through the sympathetic nervous system but was due to direct action of angiotonin on the blood vessels themselves. One wonders, therefore, whether failure of a hypertensive to respond to the methonium compounds should not cause attention to be directed to a possible ischaemic kidney as cause of the hypertension. This case will be reported in detail later.—I am, etc.,

Sydney, Australia. ZELMAN FREEMAN.

Toxic Chemicals in Agriculture

SIR,—We support the view expressed by Drs. I. A. MacDougall and K. Vickery (April 28, p. 949) that strict control should be exercised in the use of toxic chemical substances in agriculture in Great Britain. Greater protection both of agricultural workers who apply these substances and of persons who consume foods which have been sprayed could be achieved by means of regulations.

Such regulations have been made and are enforced by law in parts of the United States of America. For example, in California it is necessary to secure a permit from the State Department of Agriculture before using toxic insecticides. Permits are issued only to persons who have satisfied this department that they will obey the regulations. Spraying must be confined to the property for which the permit is sought, and the holder agrees to refrain from using toxic substances in places where persons or animals may be affected by the spray. It is necessary to give warning of spraying to all people on the property and to take measures to protect them from harmful effects. Sprays must be used only in concentrations and for the purposes approved by the State Department of Agriculture. Toxic substances must not be applied when the wind velocity exceeds five miles per hour. Special regulations are designed for the protection of bees and of livestock and other animals. When more than 1 lb. of "parathion" is applied per acre, warning notices must be posted in the area for 14 days.

Toxic substances must be registered by the State Department of Agriculture before they are sold for use within the State. A substance is not accepted for registration unless it can be proved that it is of practical value when used as recommended by the manufacturer. The product must be distributed in containers which enable it to be handled safely, and regulations ensure that the nature and toxic properties of the ingredients appear on the label of the container. The authorities in a given State may inspect fresh market produce and determine in the case of any item the presence and concentration of spray residues. By this means it is possible to detect evasion of the State regulations for the safe use of toxic chemical substances in agriculture, and to ensure that food is not contaminated by dangerous amounts of such substances.

We are aware that manufacturers and contract sprayers in this country have done a great deal to reduce the potential hazards associated with the use of toxic substances made and used to increase food production. Nevertheless in our opinion the use of toxic chemical substances in agriculture in Great Britain should be controlled by regulations which are enforced by law.—We are, etc.,

London, E.1. P. LESLEY BIDSTRUP.
DONALD HUNTER.

Varicella and Herpes Together

SIR,—It is a common experience to find varicella occurring in contacts of cases of herpes zoster, and more rarely the reverse, but it is very unusual to find them present together in the same patient. This has prompted me to record a case which came under my care recently.

A gravedigger, aged 47, first saw me on August 29, and complained of a continuous severe pain spreading over the left shoulder and down the front of the left arm. He tried to carry on at work, but two days later the pain was so severe that he willingly gave up. On the evening of September 2 he first noticed "blisters" on his left arm when he rolled his sleeve up, and the following morning found them generalized. On examination at this time there was a typical herpes zoster eruption involving the cutaneous distribution C8 and T1, and also a generalized eruption typical of varicella. There were many vesicles on the scalp, trunk, and limbs, a few on the face, but none on the mucous membranes. Successive crops of vesicles occurred on the trunk over the following two days. The patient had a temperature of 99° F. (37.2° C.) which fell to normal next day. The pulse rate was 72 per min. The tendon reflexes were present and equal. The vesicles became slightly purulent and crusted in the usual way.

On September 10 he complained of some weakness of the left arm, and the muscles were tender on pressure. There was no sensory loss. The varicella crusts were separating but not the herpetic ones.

On September 14 he complained of a great deal of pain over the left shoulder and down the front of the left arm. He was not sleeping well because of an intense smarting over the area of the herpetic eruption. Some crusts had separated, and he stated that the arm was more painful since this had occurred. There was marked hyperaesthesia over the area of the herpetic eruption. By September 21 the varicella crusts had practically all separated, though there were still many of the herpetic crusts left. The pain in the shoulder and arm was now easing off. From this time there was a steady improvement in the pain and by October 7 the crusts had all separated and the patient felt well enough to return to work.

It is usually stated that when the two eruptions occur together there is an interval of three to five days after the appearance of the zoster rash during which the virus spreads from the posterior nerve roots into the blood stream, and then the rash of varicella appears. In this case it was present within twelve hours.—I am, etc.,

Macclesfield. E. G. L. MARK.

Phlegmonous Enteritis

SIR,—The report by Mr. B. C. Rowlands (April 28, p. 926) of a case of phlegmonous enteritis following an operation for strangulated femoral hernia prompts me to record briefly two cases which I have encountered in recent weeks. Both presented as intestinal obstruction, were diagnosed at operation as Crohn's disease, showed naked-eye changes in the gut almost exactly as described by Mr. Rowlands, but were proved histologically to be periarteritis nodosa.

Case 1.—A woman, aged 50, was admitted with acute intestinal obstruction. She gave a history of frequent attacks of abdominal pain, distension, and vomiting during the preceding two months. At laparotomy the terminal ileum was inflamed and oedematous for a distance of 8 in. (20 cm.). The abdomen was closed without further interference. Her condition did not improve; on the 10th day she developed anuria and died in uraemia two days later. At necropsy the kidneys showed the typical appearance of the microscopic form of periarteritis nodosa, with widespread "explosive" glomerular lesions and fibrinoid necrosis of some afferent arterioles. Necrotizing arteriolar lesions were also seen in the spleen and in the submucosa of the inflamed ileum.

Case 2.—A woman, aged 69, was admitted with acute intestinal obstruction. There had been two short attacks of threatened obstruction during the preceding three weeks. At operation the descending colon was inflamed and oedematous in its middle 4 in. (10 cm.). The colon was resected from mid-transverse to sigmoid, followed by end-to-end anastomosis. Following operation, obstruction persisted, necessitating a caecostomy on the third day. This was closed on the 15th day, normal bowel function having returned, and further progress was uneventful. The affected gut presented the following features. The mucosa was deep red in colour and covered with minute superficial erosions for a distance of 4 in., being sharply demarcated from the normal mucosa at either end. The submucosa was intensely oedematous, accounting for most of the swelling of the bowel wall. On histological examination the small vessels in the submucosa beneath the mucosal erosions showed a necrotizing lesion typical of the acute phase of periarteritis nodosa.

Although Mr. Rowlands describes the naked-eye appearance of his specimen in some detail he makes no mention of histological examination. In the light of my two cases I would consider a diagnosis of periarteritis nodosa in any case of supposed acute Crohn's disease or phlegmonous enteritis, and it is a diagnosis which can be made only histologically.—I am, etc.,

Rochester, Kent. R. B. H. TIERNEY.

Benign Calcified Epithelioma

SIR,—Mr. John Ll. Temple's article (April 28, p. 920) on the benign calcified epithelioma of Malherbe will direct attention to this lesion, which, as he says, is not uncommon but frequently goes unrecognized. It may therefore be of interest to record a further series of ten cases encountered among 9,950 miscellaneous surgical specimens from general hospitals examined histologically during a total period of six years.

The details summarized in the table show the series to be closely similar to Mr. Temple's, save that giant-cells were found in every case, neither bone formation nor pigmentation was observed, and a history of injury was obtained in one case only. It should also be recorded that there was local recurrence in Case 2 seven months after excision (possibly incomplete), and that cell-masses of the basal type showing a number of mitotic figures were found in Cases 1, 2, 5, and 7, all of which appeared to be early lesions which had undergone relatively little calcification or even none at all. In the present series viable epithelium was present in seven cases; in Case 8 the cell masses surrounded a well-defined epidermoid cyst.

Ten Cases of Benign Calcified Epithelioma. Giant Cells Were Present in All, but Pigment and Bone Formation Absent

Case No.	Sex	Age	Site	Injury	Clinical Diagnosis	Viable Epithelium	Calcification
1	F	14	Shoulder	–	? Dermoid cyst	+	+
2	F	?	Eyebrow	–	Sebaceous cyst	+	+
3	F	13	Neck	–	Tuberculous gland	+	+
4	F	46	Abdomen	–	Subcutaneous tumour	–	+
5	M	12	Leg	+	Thrombosed vein	+	+
6	F	4½	Neck	–	Sebaceous cyst	–	+
7	M	9	Neck	–	Tuberculous gland	+	–
8	M	40	Chest	–	Cyst	+	+
9	F	67	Arm	–	Cutaneous tumour	–	+
10	M	40	Shoulder	–	Cutaneous tumour	+	+

The aetiology of the condition cannot be regarded as established, but it would seem that proliferation of basal cells is an element which cannot be entirely discounted.—I am, etc.,

Portsmouth. R. D. CLAY.

SIR,—Mr. John Ll. Temple has drawn attention (April 28, p. 920) to a condition that hardly merits the term epithelioma, since it appears to be more closely related to implantation dermoids. It is noteworthy that the latter are more commonly seen on the hands and feet, where there is a much thicker layer of skin, than on those parts which are the usual sites of benign calcified epithelioma.

I have recently seen the sections of one such case, which occurred in a girl of 5 years and underlay a vaccination scar on the arm. The lump had been present for two years; spherical in shape, about 1 cm. across, attached to the skin, and firm in consistence. A provisional diagnosis of implantation dermoid was made. The histological section showed its true nature. Pathologists appear to be more familiar with this condition than surgeons.—I am, etc.,

London, S.E.1. KENNETH MALCOMSON.

SIR,—I read with interest Mr. Temple's article on benign calcified epithelioma (April 28, p. 920). The one important differential diagnosis of this condition is from a calcified epidermal cyst, and the criterion for differentiation is the presence of squamous epithelium and the absence of basophilic cells in the latter. "Ghost" or "shadow" cells, calcification, and ossification occur in both. In so far as Mr. Temple was able to find only squamous epithelium in his series, it would appear that his cases were in fact calcified epidermal cysts and not benign calcified epitheliomata. The latter probably arise from primary epithelial germ cells with a tendency to differentiate into keratotic hair cells, and in them the shadow cells can be seen originating from basophilic cells (Lever, W. F., and Griesemer, R. D., 1949, *Arch. Derm. Syph., N.Y.*, **59**, 506).—I am, etc.,

London, W.1. PETER BORRIE.

The Tuberculosis War

SIR,—Mass radiography can, and does, play a useful part in tuberculosis control. The question, however, is whether mass radiography ought not more often to essay surveys conducted along research rather than the usual routine lines; or, at least, to combine these two aspects of the mass surveys.

In the Rhondda Fach valley an attempt to survey as near 100% as possible of the mining and non-mining population of this valley has just been made, with special arrangements for the rapid hospitalization of existing and newly discovered cases. Those unfit, for one reason or another, for hospital treatment are being trained to reduce their infectivity to a minimum, through domiciliary visits by a very able and tactful health visitor. It is reasonable to expect that such efforts—continued at intervals over a period of five years—will reduce the amount of active tuberculosis and certainly the degree of communal infection in this area very considerably. The big question remains, however: Can such an effect be made a permanent feature of this mining valley?

The answer must be no—unless the efforts being made on medical lines are paralleled by providing what Dr. Brailsford has described as "improvement in the housing of the people . . . and the provision of good, fresh, wholesome, nourishing, cheap food," adequate rehabilitation facilities for the tuberculous persons discovered and treated under such a scheme, and an adequate number of houses at cheap rent. To engage in continually expanding military preparations, and at the same time to attempt to "wipe out tuberculosis in a generation," are, however, mutually exclusive aims.—I am, etc.,

Cardiff. T. FRANCIS JARMAN.

Streptomycin and Tuberculous Meningitis

SIR,—The article by Drs. W. C. Calnan, J. Rubie, and A. F. Mohun in the *Journal* of April 14 (p. 794) prompts me to put the following question to them and to any other colleagues who have in their practice cases of cured tuberculous meningitis: Has insomnia been noted as an after-effect of the disease? I have in my practice a girl of 20 who made an excellent recovery after prolonged treatment with streptomycin and hospitalization. She is now to all clinical appearances a healthy young woman, having been discharged from hospital over a year ago, and is back at work. But she simply cannot get off to sleep without a full dose of barbiturates. All devices have been tried to enable her to sleep without the use of these drugs, but the fact remains that nothing except full doses of barbiturates have the desired effect.—I am, etc.,

Plymouth. CHARLES WESTON.

Pethidine Sensitivity

SIR,—The correspondence in your columns following Dr. D. Zuck's memorandum on pethidine sensitivity (January 20, p. 125) was forcibly brought back to me recently by a case showing even greater sensitivity to this drug.

The patient, a woman of 43, was of medium build, weighing 120 lb. (54.5 kg.), and had had no previous illnesses of any importance. Routine examination showed no pulmonary or cardiovascular abnormality. Her pre-operative blood pressure was 130/75 mm. Hg. She was to be operated on for moderate prolapsus uteri. Premedication was by papaveretum ¼ gr. (22 mg.) and scopolamine 1/150 gr. (0.43 mg.) three-quarters of an hour pre-operatively. Induction was by 5% thiopentone (0.6 g.), an oral airway being inserted (and anaesthesia being maintained by nitrous oxide 5½ litres per minute and oxygen 1½ litres per minute). Once the gas-oxygen sequence was established, 25 mg. pethidine (0.5 ml.) was given into the dorsal vein of a hand, taking about 10 seconds for the injection. As a towel clip insertion shortly after resulted in a marked facial pain reaction and generalized stirring, a further 25 mg. was similarly given about three minutes later.

The operation thereafter proceeded satisfactorily, was of 45 minutes' duration, and the blood loss less than half a pint (280 ml.). Occasional assisted respiration was necessary throughout, as the respiratory rate was rather slow. Throughout the patient was of good colour with a full regular pulse of around 80 per min. The airway was removed at the conclusion of the operation, as the patient would not tolerate it, and she was returned to bed on her side. Fifteen minutes later a hurried call from the ward was made. The patient was found blue-grey, pupils dilating, extremities cold and clammy, no peripheral pulse, capillary refill time as far as hands and ears were concerned non-existent; a worried attendant stated that "she went like this all at once." A very slow apex beat of just below 50 per min. just audible with care and an occasional deep gasping respiration (of about 5 per min.) were the only signs of life.

Immediate resuscitation, consisting of a rapid plasma drip, intravenous 5 ml. nikethamide, continuous oxygen therapy, and lowering the patient's head, was instituted. Recovery was not marked and for a few hours the outlook was bleak. Three hours after commencing resuscitation the pulse had risen to 60 per min., the respiratory rate to 10 per min., the blood pressure to 85/?, the pupils had contracted, and the patient was just conscious. Nine hours after operation the pulse was 80 per min., respirations 16 per min., while a systolic pressure of over 100 mm. Hg was recorded. The fourth pint of plasma was by this time being used. From this point her recovery was uneventful and she was up on the fifth post-operative day. No evidence, incidentally, of any weals was noticed at the site of the pethidine injection; subsequent sensitivity tests have not been carried out.

The points of importance in this case, I feel, are: First, that owing to the slowing of both the heart rate and the respiration pethidine is most likely to have been the cause of the acute generalized shock; secondly, that without immediate resuscitation a fatal termination would appear to have been a foregone conclusion—and this with a total dose of 50 mg. intravenously and divided at that. The other points of interest appear to be that this collapse, while sudden in onset, occurred after the patient was returned to bed, and that the state of shock appeared to last considerably longer than that of a straightforward surgical trauma resuscitated by similar methods.

There appears to be little doubt that individuals vary in enormous degree in their reaction to this drug when given intravenously as opposed to the intramuscular route. (I only the previous day administered 200 mg. pethidine in divided doses together with gallamine triethiodide and gas–oxygen to a young girl for a straightforward appendicectomy.)

Subsequent very guarded use of the drug on my part has been with a solution of 100 mg. in 10 ml. normal saline, keeping rigidly to a maximal intravenous injection rate of 1 ml. per minute. Until we know more accurately the mode of action, and especially the physiology of elimination, I feel that intravenous pethidine has little place as a routine anaesthetic agent.—I am, etc.,

Norwich. A. L. REYNARD.

First Mention of Rickets

SIR,—As one of those who heard Dr. Hugh Sinclair's interesting address on the history of nutrition at the recent Osler Club meeting (April 14, p. 816), may I be permitted to draw attention to an early English reference to rickets which, so far as I know, has not yet met the eye of the historian of that disease?

It occurs in a book by the learned seventeenth-century divine Thomas Fuller (1608–61) and runs as follows:

"There is a disease of infants (and an infant disease, having scarcely as yet gotten a proper name in Latin) called the Rickets; wherein the head waxeth too great, whilst the legs and lower parts wane too little. A woman in the west hath happily healed many by cauterizing the vein behind the ear. How proper the remedy for the malady I engage not, experience ofttimes outdoing art, whilst we behold the cure easily effected, and the natural cause thereof hardly assigned.

"Have not many nowadays the same sickness in their souls? their heads swelling to a vast proportion and they wonderfully enabled with knowledge to discourse? But, alas, how little their legs, poor their practice, and lazy their walking in a godly conversation! Shall I say that such may be cured by searing the vein in their head, not to hurt their hearing, but hinder the itching of their ear?"

The passage is to be found in Meditation 19 of Fuller's *Good Thoughts in Worse Times*, printed in London by W.W. for J. Williams in 1647, which is a continuation of his *Good Thoughts in Bad Times*, printed in Exeter in 1645. Fuller had been living in Exeter as chaplain to the infant princess Henrietta. His accurate description of the physical appearance of rickets, which indicates that he had seen actual cases, and his allusion to the "woman in the west" support Glisson's statement that it was in that part of England that the earliest cases were noticed.

As the first record of the English word "rickets" the Oxford Dictionary quotes the title of Daniel Whistler's Latin thesis (Leyden, 1645) and then a line from J. Whitaker's *Uzziah* (1646), "The disease called the Rickets in tender children." For the first figurative use of the word it quotes Fuller's *Worthies* (1661). It would appear that the passage quoted above contains the first accurate and precise definition *in English* of rickets and merits inclusion in the Oxford Dictionary, while the account of "spiritual rickets" antedates the 1661 reference to the figurative use of the word by fourteen years.—I am, etc.,

Wellcome Historical Medical Library, London N.W.1. F. N. L. POYNTER.

Methyl Thiouracil and Anginal Pains

SIR,—In the Refresher Course on "Coronary Artery Disease" (April 21 and 28, pp. 874 and 937) Dr. A. Rae Gilchrist does not mention thiouracil in the treatment of angina pectoris or coronary insufficiency. For the past four years I have been treating with methyl thiouracil some twenty patients suffering from severe anginal pains. The series is small and the time of observation too short to reach any final conclusion, but all my patients appear to have benefited from this treatment. Methyl thiouracil

in doses of 200 or 100 mg. daily is tolerated well even for many months. Apart from an easily controlled tendency to gain weight I have not yet met with any untoward effects. At the same time it is important to remember that this, like most active drugs, should be used with discretion owing to the possibility of a number of toxic effects. While, therefore, further investigations are necessary to clarify the mode of action and the actual degree of efficiency of this treatment, the result observed so far justifies its use in selected cases.—I am, etc.,

Carshalton, Surrey. WILLIAM N. ROGERS.

Danger of End-to-side Uretero-colic Anastomosis

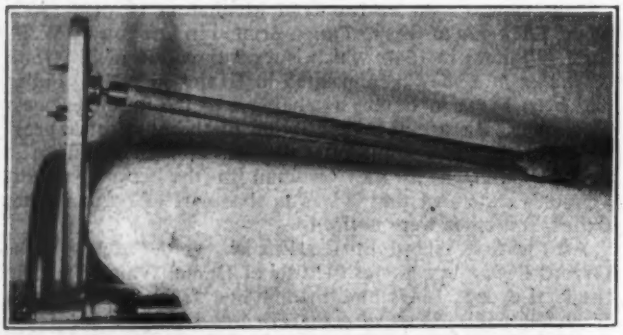
SIR,—Some three years ago the end-to-side anastomosis of the ureter to the colon was described. In the press and elsewhere I have advocated this operation because of the ensuing rapidity and certainty with which urine is excreted into the bowel. We have, however, been dismayed by the subsequent occurrence of intermittent ascending infection in too high a proportion of cases. This appears to be due to reflux. A careful study is being made and will soon be ready for publication. In the meantime, I should like it to be known as widely and as quickly as possible that our experience suggests that the method is unsafe and our opinion is that it should not be employed.—I am, etc.,

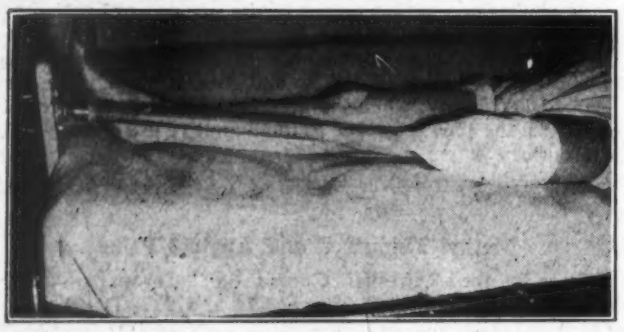
Liverpool. CHARLES WELLS.

A Substitute Prosthesis for Use in Bed

SIR,—The wearing of an artificial limb often brings relief of unpleasant sensory manifestations (the phenomena of the phantom limb), and of untoward motor effects (jactations of the stump) in patients after leg amputation. To make use of this fact so that patients' sleep need not be unnecessarily disturbed, a substitute prosthesis for use in bed was devised.

It consists of a pole with a conical expansion at one end, and a ball and socket swivel attached to a vertical piece of wood at the other so that it can be fixed to the foot of the bed (see photograph). A plaster shell is made around the conical expansion to fit the patient's stump. By raising the





top of the bed and placing the stump in the plaster shell, a constant pressure is maintained on the end of the truncated leg, simulating the effects of a prosthesis. The swivel allows the patient to turn over comfortably in bed.

So far the appliance has been used only on two chronic sufferers from sensory manifestations; they were under the care of Dr. W. Ritchie Russell. The first had a painful phantom, which was worse at night after removal of his prosthesis. He gained considerable relief, and took his model home when he left hospital. The second had radiation of pain from the phantom and stump to the lumbosacral region, groin, and scrotum, and, as was anticipated, obtained little relief.

I describe the appliance in the hope that those who have to deal with amputation, particularly in the early stages, may consider it worthy of trial. I am grateful to Dr. W. Ritchie Russell, and the Director-General of Medical Services, Ministry of Pensions, for permission to publish this description.—I am, etc.,

Stoke Mandeville. J. E. A. BARTLET.

Strangulated Hernia in Infant

SIR,—On reading the case history of the strangulated inguinal hernia in a 7-weeks-old child by Professor Francis E. Stock (January 27, p. 171) and noting the comment made regarding the 10 days of comparative well-being experienced by the child while intestinal strangulation and sloughing were taking place, I felt that the following record of a mildly similar case might prove of interest.

A West African girl approximately 3 weeks old was admitted to a mining hospital in Sierra Leone Northern Territories with a twisted loop of transverse colon, which was ruptured, protruding through the umbilicus; nothing was being passed by rectum. The child was fat, looked healthy, and weighed 7 lb. (3.2 kg.). The mother stated that the intestines had protruded following the ministrations of a native midwife, and a suture had been placed round them and tied. An attempt was made under open ether anaesthesia to reduce the hernia and repair the abdominal wall with the idea of leaving an umbilical fistula until such time as the child was old enough to stand a resection operation; but within a week the intestines were once again through the umbilical aperture. A second attempt was made and this time the adjoining loops of intestine were separated. A large hole (about 2.3 cm. across) in the transverse colon was repaired in two layers and the abdomen closed in layers under open ether anaesthesia. The child became very shocked and was not thought likely to survive the operation, but the following day it started to feed (breast-fed) as usual and passed faeces for the first time rectally since birth.

The improvement continued for three days and the infant was put on systemic penicillin and sulphaguanidine orally (aureomycin was not available). On the third day it developed a high temperature and fast pulse, vomited once copiously, and died. Post-mortem findings showed a generalizing peritonitis spreading from the site of operation and presumably due to a slight leakage at the repaired aperture or resulting from the original soiling.

I submit this account because of its peculiar aspects and the amazing recuperative capabilities of this particular infant.—I am, etc.,

Sierra Leone. J. T. CANTWELL.

Headache

SIR,—It is not generally realized that a frequent cause of present-day headache is the prolonged use of barbiturates prescribed either for insomnia or for "nerves." Utility psychiatry, which appears to consist in merely giving phenobarbitone and "amytal" tablets, is also responsible.

But headache after head injury is one of the most difficult symptoms to evaluate and treat, as the usual clinical features which help to differentiate organic from functional headache become obscured by repeated questioning and investigations. In medico-legal cases it makes very little difference to judges or juries whether the ache is physical or psychological in origin, but when plaintiffs have complained of persistent headache juries have been known to recommend heavier damages than they might otherwise have done in the absence of this symptom. The case is, however, different when disability pensions and claims for war pensions are concerned. If injustice to the ex-Service man or woman (and unfairness to the taxpayer) is to be avoided it is essential to assess the nature of the headache at the very outset. Unless this is done claimants for pensions are likely to be subjected to frequent investigations and repeated

lumbar punctures. These procedures have caused many a stable person to become neurotic, and tribunals are often puzzled by the conflicting opinions given by medical experts. Unfortunately, there is as yet no objective way of differentiating organic from functional headache to the satisfaction of the patient. The hopes at one time entertained that perhaps histamine might be useful in this connexion have not materialized.

In 1940, Theodore von Storch reported (*Arch. Neurol. Psychiat., Chicago,* **44**, 316) that histamine was a useful drug for distinguishing migraine from other forms of recurrent headache. A year later, experiments were conducted on volunteers at the Mill Hill Emergency (Maudsley) Hospital to determine whether histamine could be used to distinguish post-contusional headache from psychogenic ache. The results, which were published in a journal (*J. ment. Sci.*, 1945, **91**, 213) which is not easily accessible to the vast majority of your readers, might be here summarized.

Seventy-five able-bodied patients, free from physical disease, volunteered for the test. Ten men who had not complained of headache were used as controls. Of the 65 men who were subject to chronic recurrent headache, 43 dated their symptoms from a head injury. In 10 the injury had been severe, involving fracture of the cranial bones and necessitating in-patient treatment for several weeks; in 33 men the injury had been mild, not causing any fracture or greater disturbance than a few minutes' unconsciousness; while 10 gave a history of accident with doubtful head injury and no loss of consciousness. In 21 of the men the injury had been sustained within the previous two years, and in 22 it had occurred more than two years before, often between ten and twelve years before. The shortest interval was three weeks. There was no history of head injury in 12 men.

When minute amounts of histamine were given intravenously according to the technique described by von Storch transient headache was reported by 23 men, of whom eight said it was similar to their habitual headache and 15 said it was dissimilar. Of 43 patients with a clear history of head injury five reported it was like their usual ache and eight said it was unlike. Among men with no history of head injury seven reported headache, of whom three said it was similar to their usual ache, but the rest did not think so. Many described their sensations as tightness or fullness of the head, numbness, "funny feeling on top of head," or as blood rushing to the head. One man complained of a feeling of tightness over the scalp "like after wearing a steel helmet," but he refused to call it a headache. There was also no correlation between the presence or absence of history of head injury and the intensity or the character of the induced headache; nor was there any relation between the latter and the neurotic symptoms complained of by the patients. Intelligence and suggestibility also appeared to affect the result. Once they got to know what was being looked for or what was the more advantageous result, it would appear in many of them.

From this research it would be obvious that the clinical descriptions given by the patients are not reliable guides to the nature of the headache. Much research is needed in this connexion to devise a suitable clinical or experimental test which can establish the presence of organic headache and differentiate it within reasonable limits from neurotic headache. Such a test might satisfy the patients and reduce the incidence of post-contusional neurosis.—I am, etc.,

Sutton, Surrey. M. N. PAI.

Duodenal Stenosis

SIR,—Mr. A. J. Hobson's report (May 5, p. 1018) on three cases of hypertrophic pyloric stenosis in the adult tempts me to record a case of duodenal stenosis in the adult which came my way last year.

This patient had been investigated at a teaching hospital for painless vomiting of recent onset in 1948. At that time she brought up no more than water and nothing abnormal was found by the radiologist, so she was reassured and discharged. The vomiting, however, continued and became more severe. As she described it, the food was pumped up and she was afraid to eat anything solid. Still there was no pain. A barium meal showed a large atonic stomach with slow emptying, but the duodenal cap was not seen. The meal was repeated, and the stomach again appeared very distended with much fluid in spite of an injection of atropine. The radiologist suggested that the cause of all this was pylorospasm associated with a duodenal ulcer, although he could not display the duodenal cap.

At operation I was able to confirm the fact that the patient had a greatly dilated stomach, but discovered that this was due to a narrowing at the junction of the first and second parts of the duodenum. I performed a retro-colic gastrectomy, and this immediately relieved the vomiting.

Dr. G. L. Robinson reported on the specimen ". . . the pyloric sphincter is greatly thinned to form a lax channel over 3 cm. in circumference. The duodenal fringe, extending 2 cm. beyond the pylorus, is also very thin-walled and narrows rapidly to form a constriction barely admitting the tip of a little finger. There is no thickening, fibrosis, or other evidence of disease in this constriction. . . . The muscular coat of the stomach is hypertrophied up to 0.35 cm. thick, the submucous coat is enormously thickened by gelatinous oedema, and the whole mucous membrane is inflamed and granular and covered in places by greyish white fibrous membrane. The macroscopic picture is that of acute gastritis associated with dilatation behind a duodenal stricture which itself has no pathology. Microscopically, acute inflammation of mucosa of stomach. No lesion seen in duodenum." I might add to Dr. Robinson's graphic account of the macroscopic appearances that the specimen could be turned inside out through the stretched pylorus.

This patient was a woman aged 63. Whether it is possible to imagine that the stricture was of congenital origin and had never previously caused any symptoms is hard to say. Supposing this were the explanation one yet cannot see why trouble should have started in later middle age, since the narrowing would not be progressive. I can find no account of any similar case in the literature. One other thought occurs to me—that this patient (and perhaps Mr. Hobson's, too) might have done just as well with a simple gastro-enterostomy. One is so accustomed to making the wider gesture that the lesser tends to be forgotten.—I am, etc.,

London, W.1. STEPHEN POWER.

Who Shall Decide Treatment?

SIR,—A month or two back the Central Midwives Board issued a circular for distribution to hospitals by the regional boards regarding the length of time a woman should be kept in hospital after delivery; this letter was signed by the secretary of the board and makes interesting reading. Relevant parts are as follows (my italics).

"I have been directed to refer to M.-of-H. 115/47 concerning the cessation of attendance after the tenth day of the lying-in period by *institutional* midwives and to inform you that the Board has resolved, that for a further period of twelve months, it will not take disciplinary action against a midwife working wholly within an institution in respect of alleged misconduct, solely on account of the period of attendance given in a case where a midwife has attended a patient . . . in labour . . . and a period of not less than ten days thereafter."

"The Board regards the discharge of patients to either their own homes *or to post-natal homes* before the tenth day as an undesirable practice."

"In the case of training-schools for pupil-midwives any system of discharge before the tenth day of the sort mentioned above will cause the Board to reconsider the approval of the institution as a training school."

This circular is remarkable and shows a complete lack of comprehension of circumstances as they are at present.

There cannot be many maternity hospitals which are not trying, to the best of their ability, to get through in the best possible way a volume of work quite outside their ideal capacity; and in so doing they and the obstetricians in charge are trying to do their best for the community. Often this means that a balance must be struck between the necessity for a safe delivery and the desirability of a long rest for each mother, and surely this must often mean, in an area where housing is poor, that the lesser of two evils is to arrange for a larger proportion of safe hospital deliveries even if this occasionally leads to a number of early discharges to homes which are below average. It appears that the Midvives Board would have us turn a blind eye to necessity in order that their ideas of an ideal and tidy lying-in period may be realized. Perhaps many of us would like to do just this if it were possible and human to do so.

Not all of us agree that all women ought to be kept in hospital for two weeks after delivery, or that it is good for them. But the board, it seems, would not only have us treat all alike and deal with all at the pace of the slowest, but would take on itself the task of forcing us to comply with its ideas, not by fair means, but by threatening to take action at some distant date against those who work with us. Who is to decide how the patients are to be treated, the obstetrician in charge or the Central Midwives Board? This is obviously the question here.

Royal Colleges and such bodies as the Central Midwives Board have got themselves into a very strong position in that, by a process of "recognition," they can enforce certain regulations upon hospitals and departments, and by their blessing or otherwise make it possible or impossible for an institution to create and maintain an efficient medical or nursing staff. This is, of course, an ideal example of power without responsibility which if it is not to be abused requires very careful use; for example, it hands to a body interested in only one thing—that is, the training of personnel—the right to say whether an institution should be efficiently staffed, or even staffed at all; and that body will have no idea of the needs of the local community and no interest in it.

In this circular from the C.M.B. we have the example of such a detached body claiming to have the right to treat patients at a distance. In this case the idea they have is that patients ought to be kept in hospital longer, which may or may not be right and has, no doubt, been decided upon from the highest motives; but we may well have a directive from this or another body later on reducing the time of stay. It may be that the Royal Colleges and the Central Midwives Board have a duty to better the standards of treatment of the patients whose conditions concern them, but this was ever done better by example and argument than by threats. And surely threats to their members and threats to the training institutions, especially when the latter can be translated into a simple statement, "Either you do what we think you ought to or we make it impossible for you to get staff," ill become a statutory body which ought to have some dignity.

Anyhow, one is tempted to ask what law or regulation gives the Central Midwives Board the power to issue such threats.

I would like to sign my name, but, as obstetrician-in-charge of a hospital which is a training school and is hard pressed for accommodation and often has to discharge patients early, I hesitate to incur the wrath of the board, not upon myself, but upon the institution.—I am, etc.,

OBSTETRICIAN.

Testing Ice-cream

SIR,—We would like to endorse the opinions expressed in the letter of Dr. W. Howard Hughes (January 20, p. 137) regarding the limitations of the methylene-blue test for ice-creams.

Observations in these laboratories of the methylene-blue test and the full bacteriological examination on 500 miscellaneous samples of ice-cream were published by Dr. G. J. Laws (with the co-operation of Mr. W. C. Dewey and Mr. C. W. Hilliard) in 1948 (*Medical Officer*, February 28, 1948). Experience since then has confirmed the view that the methylene blue, although a useful sorting test, is not nearly as reliable and informative as the bacteriological examination as an indication of the conditions of manufacture and the hygienic quality of the product as sold to the public.

Your annotation (December 23, 1950, p. 1431) includes the following sentence, "The methylene-blue test has been criticized because its results could not be related with those of the plate-count and coliform tests, but in view of the variable results given by the latter any close correlation would be surprising." In our opinion variable bacteriological results appear to arise from unsatisfactory methods employed in the sampling, transportation, or examination; the following details of technique based on long experience in these laboratories may therefore be of general interest.

The sterile jar or bottle for the collection of the sample should be large enough to receive it complete with wrapping, etc. We consider it essential for the sample to arrive at the laboratory in a frozen condition, and the jar should therefore be packed in an effectively insulated case, with a separate vessel containing solid carbon dioxide (or ice and salt). On arrival it is stored in a conservator until 3.30 p.m., when the frozen product is removed from its wrapping and transferred with aseptic precautions to a sterile jar in which it is allowed to melt. The melted sample is mixed and then withdrawn in a sterile graduated 10 ml. pipette, any cream on the exterior of the pipette being removed by rotating it against the side of the jar. The pipette is used to introduce the necessary quantity to remain at the 10 ml. mark in the reductase tubes for the methylene-blue test after the tubes have been inverted for mixing. The pipette reading is greater than 2 ml. due to the "overrun."

For the bacteriological examination the volume measured with the same pipette is five times that for the methylene-blue test, and it is added to 90 ml. of sterile water or Ringer's solution. This 1:10 dilution is thoroughly shaken and then used to prepare the agar plates (37° C.) and MacConkey broth cultures (10 ml. of the 1:10 dilution into double-strength broth for 1 ml. quantities; 1 ml. into single-strength broth for 0.1 ml., and corresponding amounts and dilutions for smaller quantities). This practice of using a minimum of 10 ml. of the sample for bacteriological examinations in these laboratories was commenced after experiments made by Mr. W. C. Dewey over 20 years ago and is, in our opinion, of considerable importance in obtaining reliable results.

Reference was made in Dr. W. Howard Hughes's letter to the limitations of the 44° C. Eijkman test for *B. coli*, and it must be appreciated that differentiation by the usual plating technique requires several days. We have, however, adapted the rapid method suggested by E. F. W. Mackenzie, E. W. Taylor, and W. E. Gilbert (*Journal of General Microbiology*, May, 1948) for the differentiation of *B. coli* Type I from Irregular VI and other organisms in water. All positive MacConkey tubes are sub-cultured into brilliant-green ox-gall peptone lactose broth and a peptone water tube, and incubated at 44° C. At the same time a MacConkey agar plate is set up at 37° C. The reference given should be consulted for details, but gas formation in the brilliant-green broth together with indole formation in the peptone water is practically specific for *B. coli* Type I.

As most positive *B. coli* primary fermentations in MacConkey broth appear within 24 hours, and the 44° C. test takes 24 hours, the result is usually available within 48 hours. Our experience for two and a half years of this 44° C. incubation method adapted to ice-cream samples has shown it to be entirely reliable as confirmed by the longer method using MacConkey agar sub-cultures. The latter gives more information on the other organisms which may also be present.

As mentioned by Dr. W. Howard Hughes, the methylene-blue test can give a negative result in the presence of intestinal organisms, and we would add that these organisms are not the most active in reducing methylene blue. We agree with observations that the general bacteriological quality of ice-creams on sale to the public has improved considerably since 1948, the improvement being in large measure due to the application of the Ice-Cream (Heat Treatment) Regulations, 1947, as well as to improved control over the hygiene of manufacture.—We are, etc.,

The Counties Public Health Laboratories, London, S.W.1.

ROY C. HOATHER.
W. A. BULLOUGH.

POINTS FROM LETTERS

Phaeochromocytoma

Dr. A. D. MCDWYER (Dublin) writes: In the valuable contribution on this subject (March 3, p. 465) there is one important point overlooked—namely, that "tumours of the phaeochrome system" in 20% of cases occur in extra-adrenal sites, in the chromaffin tissue of paragangliomata (Goldenburg *et al.*, *J. Amer. med. Ass.*, 1947, 135, 971).

Stab Wound of the Heart

Mr. RICHARD WARREN (Weston-super-Mare) writes: I was much interested in reading the account of this condition given by Mr. G. S. M. Wilson (March 10, p. 511). . . . I have been involved in two such cases some years ago at the London Hospital and did in fact publish the one I did myself in 1910 (*Lancet*, 1914, 2, 835) . . . [the other was] in 1903, when I was house-surgeon to Mr. Percy Furnivall . . . I think he should have the credit of being (perhaps) the first in this country to suture a stabbed heart successfully.

Obituary

Sir ALBERT COOK, C.M.G., O.B.E., M.D.

A. T. S. writes: May one who had the great privilege of working with Sir Albert Cook for fourteen years add his tribute to your note (May 5, p. 1021)? Cook was "first and foremost a missionary," as you say, but this to him meant the sincerity of a prayerful student of his Master. His was no weak-kneed faith, but one which was robust yet tolerant, practical yet humble, and with it all went the greatest efficiency in his medical work. Nothing but the best possible work was good enough for the Christian doctor, serving his Lord as a doctor, though his countless patients will recall those quiet words of spiritual counsel which always came at the close of a visit to his consulting-room.

There are, however, two other pictures of Cook that should survive. One is of his gaiety and wit. One often still chuckles over a flashing comment or repartee of his—the sort of brilliantly witty thing a lesser man will think of in his bath the following day—or an anecdote so well told that the scene lived before us. There was, though, a drawback in his deplorable habit of quoting Browning on every conceivable occasion. The second picture is that of the voracious reader. Cook was a classic before he took up science, and his tastes were astonishingly varied, yet with it all he had a truly photographic memory for the printed word. Many a time during a discussion, whether of affairs or of a medical case, he would rise from his chair and go unerringly to his crowded bookshelves to take up a book and open it almost at the very page of an article read perhaps years before. His discipline of reading—almost every new medical book or fresh edition came to him—meant, however, that he kept "modern" in the best sense; although he so seldom returned to England, while his many bookshelves were generously open to every colleague and friend, whether missionary, Government, or other, who came to his delightful home at Makindye with its magnificent views over Lake Victoria.

Yes, Sir Albert Cook was, as you say, a great missionary and a great Englishman. He was also a wise, lovable, and staunch friend.

G. M. STEPHEN, M.B.

Dr. George M. Stephen, a consultant pathologist to the North-west Regional Hospital Board, died at his home in London on May 2 at the age of 41.

George Mackie Stephen, the elder son of Dr. John H. Stephen, of Aberdeen, had a brilliant academic career. He was Dux of Aberdeen Grammar School at the age of 16, took first-class honours in classics at Aberdeen University four years later, and graduated M.B., Ch.B. in 1935 with first-class honours and the John Murray Prize for the most distinguished graduate of his year. After a year of hospital work he was awarded first the Philipps Scholarship in Materia Medica and then the Thompson Travelling Fellowship, when he worked for a time with Professor H. M. Turnbull at the London Hospital. From 1938 to 1942 he was a lecturer in bacteriology with Professor J. Cruickshank at Aberdeen University and was then appointed assistant pathologist to the Essex County Council with charge of a laboratory at Broomfield Hospital. In 1944 he was appointed assistant pathologist to the L.C.C. North-western Group Laboratory, where he worked until 1947, when he developed a severe attack of infective hepatitis which kept him off duty for many months. Although he was back at work for nearly two years he never completely recovered from this infection.

Dr. Stephen was a man of outstanding intellect, but ill-health prevented him to some extent from fulfilling the early promise of a brilliant postgraduate career. He was a competent hospital pathologist with a particular interest in bacteriology and a sound knowledge of general medicine. A man of culture and catholic interests, he had great fluency in both the spoken and the written word and was an excellent teacher. Many students will remember his witty sallies which drove home the dull facts. Besides possessing a deep knowledge of music, he had a good tenor voice. He was a devout churchman. His wide circle of friends will miss him sorely, for he was a most likeable man. He leaves a wife and two children, to whom we extend our deep sympathy.

Medical Notes in Parliament

National Health Service Bill

The Bill was considered in committee in the House of Commons on May 2, with Major J. MILNER in the chair. Mr. E. H. KEELING moved an amendment proposing that foreigners should pay the full cost of any teeth or glasses they obtained in this country.

Mr. H. MARQUAND replied that the amendment was not necessary to achieve the object they had in mind, as he and the Secretary of State for Scotland had the power to charge such people. He pointed out that they had not yet done so because there were grave administrative difficulties in the way, and he did not think that the compulsory showing of identity cards to prove the patient's right to the benefits of the Service would be satisfactory.

Mr. A. BEVAN, speaking from the back bench he has occupied since his resignation from the Government, opposed the amendment, saying that if they accepted it there would be no logical reason why they should not charge for all medical treatment. He said that visitors did not come to this country to have an accident, and he considered it a natural piece of hospitality for the British people to care for them. He went on to speak of abuses in the Service, referring to the "manipulation of fee-paying beds by specialists in hospitals."

Dr. CHARLES HILL did not think that the visitor to this country regarded it as necessary or reasonable that part of our hospitality should be the provision of free teeth and glasses. The question was put and the amendment rejected.

Mr. F. MESSER moved an amendment stating that anyone under medical treatment, either at home or in any institution, should be entitled to free dentures. Mr. A. BLENKINSOP said that he sympathized with the point and promised to look into the matter. Mrs. E. BRADDOCK disliked the whole Bill except for the section on tuberculosis, and said that if charges were to be made they should be equitable. Mr. EMRYS HUGHES believed the provision for tuberculosis patients to be good, but thought the rest of the Bill was rotten and reactionary.

Mr. BLENKINSOP promised to try to arrive at a clearer definition in regard to patients undergoing treatment, and the amendment was withdrawn.

MEANS TEST

Mr. ELLIS SMITH then moved that any person whose gross income before deduction of income tax did not exceed £8 per week should be exempted from payment. He thought

that the proposed payments should not be accepted until the suggestions made in the Civil Appropriation Accounts had been carried out and the proposals made by the Auditor-General had been considered. Miss J. LEE felt that the Bill was mean and cruel, and that by the amendment they could make it a little less so. Mr. H. MCNEIL pointed out that such essential services as the number of beds for tuberculosis patients were being extended, quite apart from the Switzerland experiment. He did not think that the figure of £8 per week would be a fair test; the amendment would prove difficult to administer, and he assured Members that needy cases were already being cared for in the Bill. The amendment was negatived.

Dr. BARNET STROSS wanted an assurance that the charges would be withdrawn on March 31, 1952, saying that if a breach of the principle of the Service were to be tolerated, it should be for as short a time as possible. Mr. MARQUAND said that it was his intention on the report stage to introduce a clause bringing the charges to an end in April, 1954. Dr. STROSS withdrew his amendment.

Dr. HILL considered that if there were to be charges they should be related to a careful examination of the Service as a whole. He did not think they ought to be planted on one kind of recipient of that service. He added that he hoped that if there was to be a further reconstruction of the dental service it would be possible to put the dental estimates work on a regional basis.

Mrs. BRADDOCK asked how the charges were to be collected, pointing out that £4 5s. was almost a week's wage in a working-class family. On the question of spectacles, she said people were being forced to go to the cheap shops which were again ready to supply glasses for half a crown.

COLONEL M. STODDART-SCOTT asked whether the provision of glasses for schoolchildren included the splinter-free type. Mr. MCNEIL replied that it did not. Answering the points raised by Dr. Hill, he explained that the Government had decided to place a charge on dentures because they did not wish to charge for the services—medical, dental, or any other kind—which might be expected to fall inside the Health Service. They thought that the fairest way to get the money they needed was by charging for appliances.

After further debate the motion that the clause authorizing charges for teeth and glasses should become part of the Bill was accepted. Clauses 2, 3, 4, and 5 were also accepted.

FINAL STAGES

On May 7 the Bill was further considered when Mr. A. BLENKINSOP moved an amendment to restrict the free provision of appliances to patients in hospital to those who had been in-patients continuously since the prescription of the appliances.

Dr. CHARLES HILL pointed out the unfairness of making people pay when for some reason their new teeth or glasses were delayed in delivery, and said that nothing should be done which would encourage old people to stay in hospital. After considerable adverse comment from other members the amendment was negatived.

Mr. H. MARQUAND then introduced the promised Clause to bring the effect of the Bill to a close in April, 1954. After some debate, in which Mr. F. G. BOWLES suggested that the Government were under pressure from the American Medical Association to modify the free Health Service, the Clause was added to the Bill.

Two other proposed amendments were shortly debated and then withdrawn, and the House then proceeded to the third reading of the Bill. This completed its consideration in the House of Commons.

Foreign Dentists

On April 26 Mr. S. S. AWBERY asked the Minister of Health what was being done to make use of the services of foreign dentists in this country who had been naturalized. Mr. H. MARQUAND said that the Government would introduce a Bill at a convenient opportunity. So far as he was aware, it would affect less than 100 foreign dentists.

Health Centre

On May 3 Mr. SOMERVILLE HASTINGS asked the Minister of Health why the comprehensive health centre which the Sheffield Health Committee decided to inaugurate in 1948 by the conversion of the Frith Park maternity and child-welfare centre was not yet in operation, and what was holding it up. Mr. H. MARQUAND said that he understood that the doctors concerned were unwilling to co-operate, and agreed to look into the suggestion to call a meeting of the doctors to put his case to them.

Specialist Fees

Asked by Mr. D. F. VOSPER on May 3 what steps were taken to ensure that hospital patients contracting for pay-bed accommodation were told in advance the amount of specialist fees, Mr. H. MARQUAND said that the fees were arranged privately between patients and specialists. Hospital authorities had been asked to draw the patients' attention to the maximum charges allowed when they signed the undertaking to pay the hospital charges.

Thames Pollution

Mr. J. A. BOYD-CARPENTER asked on May 3 whether Mr. Marquand was aware of the pollution of the River Thames; and whether, in view of the opening of the bathing season, he had any statement to make about dangers to health involved in bathing in this river. Mr. H. MARQUAND said that above Teddington the risks to bathers were not great. The Minister of Local Government and Planning informed him that to purify the Thames completely would cost more money, materials, and labour than the country could afford at present. It was impossible to measure accurately the risk to health, and he could only give a general opinion based on that of his medical advisers.

Pay-beds

Major TUFTON BEAMISH on May 3 asked the cost of a bed in a single-room private ward in the Victoria Hospital, Lewes, how this compared with the cost of a similar bed in 1938, the main reasons for the increase in cost, and what was the profit or loss on the administration of all beds in private wards, excluding services rendered by medical practitioners, during the last financial year. Mr. H. MARQUAND gave the present cost as £18 11s. per week, excluding medical fees, compared with from 4½ to 8 guineas in 1938. He said that the increase was due to increased hospital costs. Exact information was not available on the last part of the question, but pay-bed charges were, under section 5 of the National Health Service Act, 1946, designed to cover the cost of the accommodation and services provided.

Hospital Waiting-lists.—On December 31, 1950, there were 553,577 people awaiting admission to hospital. The number now on the waiting-list is less than it was a year ago.

Health Service.—There are 468 hospital management committees and boards of management in England and Wales and Scotland, controlling 2,875 hospitals.

National Hospital Service Reserve.—The number of recruits enrolled is now 14,675. Since in the event of war the hospital and first-aid services would need about 80,000 additional nurses, Mr. Blenkinsop does not regard the present rate of progress as satisfactory.

Modifications have been made to the memorandum prepared by the Board of Control on the licensing of mentally defective patients from institutions. When a woman subject to an order or authority for detention under the Mental Deficiency Acts is found to be pregnant a report should be made to the Board of Control, and never to the local police. Should the question of criminal proceedings arise it will be the responsibility of the Board to submit the papers to the Director of Public Prosecutions, who will communicate with the police.

Medico-Legal

AN UNUSUAL ETHER EXPLOSION

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

The hazards of explosion of ether vapour and similar substances by a spark from an electrical apparatus or a static discharge are well recognized and guarded against, but empty ether bottles have hitherto not been considered dangerous. A fatal accident which occurred at the Kent and Canterbury Hospital at the beginning of February proved, however, that they constitute another serious risk in the operating theatre. An elderly patient was undergoing a mouth operation under trilene anaesthesia, and just after the surgeon had made one incision with the diathermy knife an explosion occurred in an empty ether bottle on the trolley. The rubber bag was set on fire and the tube leading to the patient's throat was disconnected. The patient stopped breathing and started to bleed from the lungs. The anaesthetist applied suction to the end of the tube and removed as much blood as possible from the lungs. A bronchoscope was passed and oxygen and nikethamide were administered, but the patient died in a quarter of an hour.

At the inquest, held on February 5,[1] the anaesthetist stated that before the operation he had verified that the ether bottle was empty, and had blown gases through the bag and tube and smelt them to make sure that they contained no ether vapour. The taps had been in proper position. He had compressed the rubber bag, and this act must have in some way drawn ether vapour from the empty bottle into the circuit. In future, empty ether bottles would be removed. The apparatus had been serviced by the manufacturers about a fortnight before the accident.

The pathologist stated that the body of the deceased showed superficial small marks of burning on the right side of the forehead and some degree of singeing of the eyebrows. Extensive interstitial haemorrhage involved nearly the whole of both lungs, and there was much blood in the trachea and bronchi. There had been long-standing emphysema and bronchitis.

The jury returned a verdict of accidental death, and recommended in a rider that the ether bottle should be removed when ether was not being used in an operation.

1 *Evening Standard*, February 5; *Daily Telegraph*, February 6.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on April 26 the following medical degrees were conferred:

D.M.—Q. J. G. Hobson, P. C. Reynell.

B.M.—Mrs. Marie L. S. Beesley, D. L. Hadley.

Professor T. N. A. Jeffcoate, Professor of Obstetrics and Gynaecology in the University of Liverpool, will deliver a Litchfield Lecture on "Incoordinate Uterine Action" in the maternity department lecture theatre of Radcliffe Infirmary, Oxford, on Thursday, May 17, at 4.15 p.m.

Richard Alfred Chambers, B.M., B.Ch., M.R.C.P., has been elected to a Radcliffe Travelling Fellowship.

UNIVERSITY OF CAMBRIDGE

In Congregation on April 28 the following medical degrees were conferred:

M.D.—D. A. W. Edwards, M. E. Moore, C. N. Pulvertaft, O. L. Wade, I. G. Wickes.

M.CHIR.—J. F. R. Withycombe.

M.B., B.CHIR.—*G. S. Brindley, *P. E. Huddy.

Applications for the Michael Foster Studentship in Physiology should reach Professor E. D. Adrian, O.M., M.D., P.R.S., at the Physiological Laboratory, University of Cambridge, by June 30. The student receives the annual income of the fund (about £120) and may be re-elected for a second year.

*By proxy.

UNIVERSITY OF GLASGOW

The following medical degrees were conferred on April 28:

M.D.—R. Paul (with commendation), D. C. Watt, T. S. Wilson.

UNIVERSITY OF LONDON

The following candidates at the London School of Hygiene and Tropical Medicine have been approved at the examination indicated:

ACADEMIC POSTGRADUATE CERTIFICATE IN PUBLIC HEALTH.—Jessie S. Freeman, H. L. Larsen, S. Mandal, K. Nagalingam, A. N. Ray, O. W. Tenfjord, Margaret O. Withof-Keus.

Professor Warren H. Cole, Professor of Surgery in the University of Illinois, will deliver two special University Lectures on "The Surgery of the Biliary System" at Westminster Medical School (Meyerstein Lecture Theatre), Horseferry Road, London, S.W., on Tuesdays, May 22 and 29, at 5.30 p.m. The lectures are addressed to students of the University and to others interested in the subject. Admission is free, without ticket.

UNIVERSITY OF NEW ZEALAND

Dr. Gerald Spence Smyth, honorary consulting gynaecological surgeon to Johannesburg Hospital, South Africa, has been appointed to the recently established postgraduate Chair of Obstetrics and Gynaecology at Auckland University College. Professor Smyth graduated M.B., B.Ch., at the University of Dublin in 1927 and proceeded M.D. five years later. He was elected a Member of the Royal College of Physicians of Ireland in 1930 and became F.R.C.P.I. in the following year. He was admitted F.R.C.O.G. in 1947. Professor Smyth will also be medical director of the Obstetrics and Gynaecology Unit at Cornwall Hospital in Auckland as well as director of the new Auckland Women's Hospital when it is built.

SOCIETY OF APOTHECARIES OF LONDON

Dr. W. S. C. Copeman has been elected to a seat on the Court of the Society in the place of Mr. R. Ogier Ward, who has resigned.

Dr. J. P. Hedley has been re-elected representative of the Society on the Central Midwives Board for a further year.

The Society's Gold Medal in Therapeutics was presented in February to Professor E. C. Dodds, F.R.S., in recognition of his eminence in the field of biochemistry.

The following candidates have been granted the diploma of L.M.S.S.A. upon examination: R. E. Hazell, J. R. C. Wallace, G. C. Stavrakis, C. B. Alvey, J. E. K. Moore, A. Ross, F. J. Covill, P. B. Hughes, W. Friis, H. G. Hexter, R. F. Mottram, P. D. Black, B. L. Breeze, A. E. H. Safeda, G. Dixon, A. L. C. A. M. Bracchi, I. W. Turnbull, T. R. P. Coakley, C. E. A. Thomas, P. Howe, K. M. Stone, Doreen G. Philipps (Viscountess St. Davids), W. M. Cornelius.

The Diploma in Industrial Health has been awarded, by examination, to C. G. Hunter.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

Professor H. L. Sheehan, Professor of Pathology in the University of Liverpool, will deliver a William Blair-Bell Memorial Lecture on "Anuria in Obstetrics" at the College House, 58, Queen Anne Street, London, W., on Friday, May 25, at 5 p.m. Admission is by ticket only, obtainable from the secretary of the College.

The Services

The *London Gazette* has announced the following appointments and mentions in dispatches in recognition of gallant and distinguished services in Malaya during the period from July 1 to December 31, 1950:

C.B.E. (Military Division).—Brigadier J. C. Collins, O.B.E., late R.A.M.C.

M.B.E. (Military Division).—Captain (temporary) G. C. Smart, R.A.M.C.

Mentioned in Dispatches.—Major J. H. Bennett, Major (temporary) T. F. Jouning, T.D., and Captain J. T. Rowling, R.A.M.C.

CASUALTIES IN THE MEDICAL SERVICES

Wounded.—Captain Thomas Dungavel, R.A.M.C.

Missing.—Captain Robert Patrick Hickey, R.A.M.C.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending April 21 (No. 16).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

Disease	1951 Week Ending April 21					1950 Corresponding Week					1942–50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	32	2	12	2	3	55	10	13	—	2	742	415	55
Deaths	—	—	—	—	—	—	—	—	—	—			
Dysentery	1,002	171	140	9	2	291	15	81	1	—	523	189	46
Deaths		2		—			—		—				
Encephalitis, acute	3	—	—	—		5	—	—	—	—	5	2	—
Deaths		—			—		—						
Erysipelas			8	3	6			23	4	8			
Food-poisoning	44	5		—		39	14		—				
Infective enteritis or diarrhoea under 2 years				11	9					15			
Deaths	16		1	—	1	18		2	—	—			
Measles*	19,025	1,211	470	198	113	6,805	174	553	378	110	15,901	9,035	2,392
Deaths		1	—	—	—			1	2	1			
Meningococcal infection	40	6	17	1		35	2	13	3	—	169	73	34
Deaths		1	—				—	—					
Ophthalmia neonatorum	41	2	14	—		39	2	20	1		101	64	39
Pneumonia, influenzal	551	22	1	16	4	659	30	6	14	—	951	728	573
Deaths (from influenza)†	16	1	1	1	2	47	7	1	4	3			
Pneumonia, primary			164					171					
Deaths	205	40		9	9	227	28		8	10			
Poliomyelitis, acute													
Paralytic	14	—	1	—		24	3	2	2	5	24	9	5
Non-paralytic	8	2											
Deaths§	1	—			—	2	—			—			
Puerperal fever			5				—	6					
Puerperal pyrexia‖	61	10	6	2	1	76	4	8	3		186	139	76
Scarlet fever	948	69	141	33	49	1,164	100	165	81	77	1,793	1,164	930
Deaths		—	—	—	—			—	—	—			
Smallpox	—	—	—	—		1	—	—	—				
Deaths				—					—				
(1) Tuberculosis, respiratory			180	45				157	38				
(2) Tuberculosis, non-respiratory			28	6				32	15				
(1) Deaths	134	27	21	3	16	204	30	30	6	6			
(2) Deaths		4	2	1	5		—	8	4	1			
Typhoid fever	4	—	1	—	1	1	—	1	—	1			
Deaths¶	1	—	—	—		—	—	—	—	—	24	8	2
Paratyphoid fever	12	1	—	—		1	—	1 (A) 1 (B)	—				
Whooping-cough	3,498	209	550	52	67	2,810	108	385	55	84	3,727	2,117	1,214
Deaths	4	—	2	—	2	6	—	—	1	1			
Deaths (0–1 year)	240	29	40	8	20	268	30	35	16	22	526	352	268
Deaths (excluding stillbirths)	5,164	858	612	148	231	5,150	817	605	146	207	5,273	4,581	4,403
Annual death rate (per 1,000 persons living)			12·4					12·2					
Live births	7,524	1,295	953	243	467	8,079	1,298	970	271	393	10,537	7,541	6,089
Annual rate per 1,000 persons living			19·2					19·5					
Stillbirths	220	25	22			227	35	30			276	239	199
Rate per 1,000 total births (including stillborn)			23					30					

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London. and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

Vital Statistics

Schoolchildren in Glasgow

Measurements of schoolchildren in Glasgow taken since 1910 show a gradual increase during the last 40 years. The average measurements of height and weight for quinquennia of children at certain ages are shown in the Table below. The data are taken from the Corporation of Glasgow's *Report on the Medical Inspection and Treatment of Schoolchildren* for the year ending July 31, 1950.

Year	5 Years				9 Years				13 Years			
	Ht. in in.		Wt. in lb.		Ht. in in.		Wt. in lb.		Ht. in in.		Wt. in lb.	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
1910–14 ..	40·0	39·9	38·5	37·9	47·1	47·2	54·0	51·7	54·5	55·0	72·8	76·4
1915–19 ..	41·1	39·4	38·5	37·5	48·0	47·5	54·6	52·1	55·9	56·0	76·1	77·3
1920–4 ..	40·5	40·1	39·1	38·0	48·5	47·9	54·3	52·8	55·1	55·9	75·0	78·2
1925–9 ..	40·8	40·3	39·1	37·7	49·0	48·7	56·7	54·6	56·0	56·3	78·2	80·9
1930–4 ..	41·1	40·8	39·5	38·0	49·3	49·1	57·2	55·1	56·4	57·3	80·1	83·8
1935–9 ..	41·46	41·18	40·08	38·59	49·90	49·63	58·57	56·68	57·22	58·16	83·12	88·00
1940–4 ..	41·95	41·57	41·26	39·64	50·49	50·17	59·99	58·09	58·13	58·85	86·55	90·79
1945–9 ..	42·14	41·75	41·67	40·06	50·85	50·35	61·16	58·94	58·30	58·98	87·23	91·80
1950 ..	42·47	42·00	42·31	40·46	51·08	50·54	61·84	59·64	58·60	59·22	88·43	93·16

Smallpox

A student from Calcutta was disembarked from s.s. *Ranchi* on April 20 at Marseilles. Modified smallpox was diagnosed. The *Ranchi* docked on May 8 in the Port of London. Warning has been sent to medical officers of health of districts to which contacts have gone.

Twenty-nine cases of smallpox have been reported in the Netherlands, 27 of them at Tilburg.

Prematurity and Foetal Deaths

The Ministry of Health has introduced a new classification of birth weights of premature infants and a special form to provide information on the weights of the foetus in abortions of 18 to 28 weeks and stillbirths, so that a comparison may be made with the weights of live premature infants according to period of survival. The form will first be used for data collected during this year.

World Incidence of Poliomyelitis in 1950

In 1950 there was a marked decrease in the incidence of poliomyelitis in Canada and the United States and an almost complete absence of manifestations of the disease in certain countries (Iceland, Mauritius, New Zealand) where in 1949 it had assumed epidemic form. On the other hand, the incidence in Europe increased, particularly in the British Isles and Scandinavia, with the exception of Sweden, and there were separate epidemic outbreaks in other parts of the world, as in Alaska, Australia, the Belgian Congo, Israel, Manila, and Panama (W.H.O. *Epidemiological and Vital Statistics Report*, January, 1951). At present, North America, the British Isles, and the Scandinavian countries are the principal foci of poliomyelitis. The report adds: "The future will show if it is necessary to include with this group such countries as the Belgian Congo, Israel, and Panama, where . . . for the first time it would appear that the disease has taken on an epidemic form."

Infectious Diseases

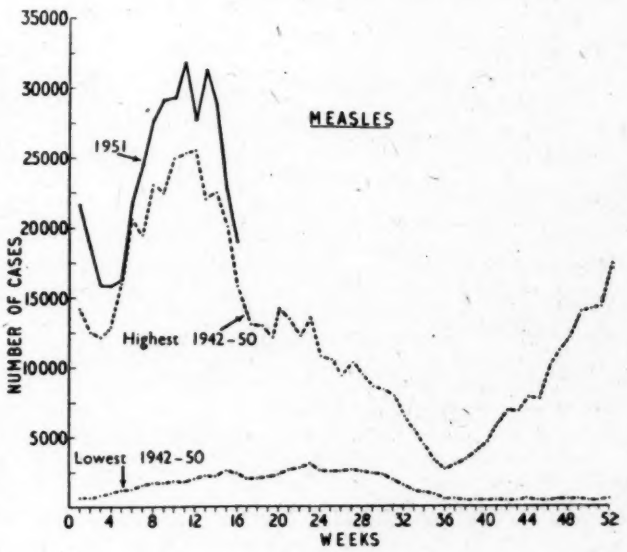
During the week ending April 21 a fall was recorded in the number of notifications of measles 3,619, whooping-cough 338, acute pneumonia 156, while notifications of scarlet fever rose by 126 and dysentery by 144.

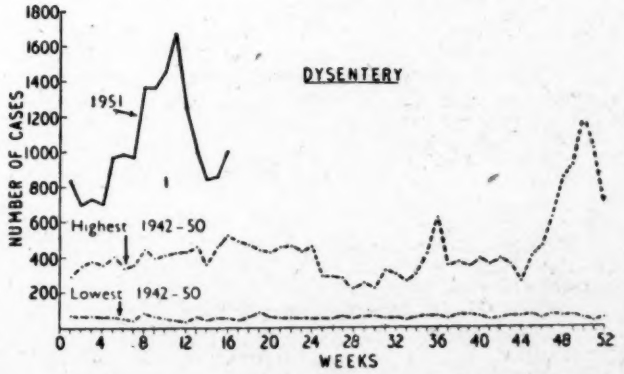
The incidence of measles greatly declined throughout the country. The largest falls in the numbers of notifications were London 399, Lancashire 395, Essex 329; the only large exception to the general trend was a rise of 105 in Durham. The largest falls in the incidence of whooping-cough were Kent 68 and London 63. The notifications of diphtheria were 10 fewer than in the preceding week and were only 2 above the lowest number ever recorded. The chief variations in the local returns of diphtheria were falls in London 5, Yorkshire West Riding 5, and a rise of 4 in Worcestershire. Small rises in the number of notifications of scarlet fever occurred in most areas of the country. Five of the 16 cases of enteric fever were notified in Lancashire, Swinton and Pendlebury M.B. Multiple notifications of acute poliomyelitis were recorded from Flintshire, Flint M.B. 3; Lancashire, Liverpool C.B. 2; Warwickshire, Birmingham C.B.2.

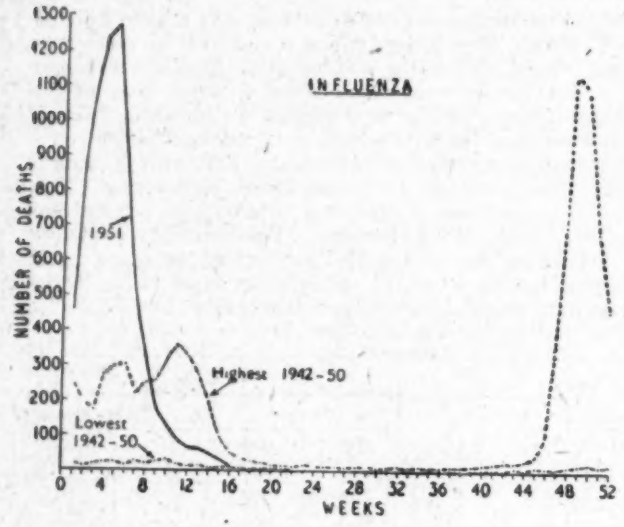
A new outbreak of dysentery affecting 39 persons was notified from Nottinghamshire, Beeston and Stapleford U.D., during the week. The notifications of dysentery in London rose by 59 to 171 and in Essex by 46 to 89. Other large returns of dysentery were Lancashire 149, Yorkshire West Riding 73, and Middlesex 71.

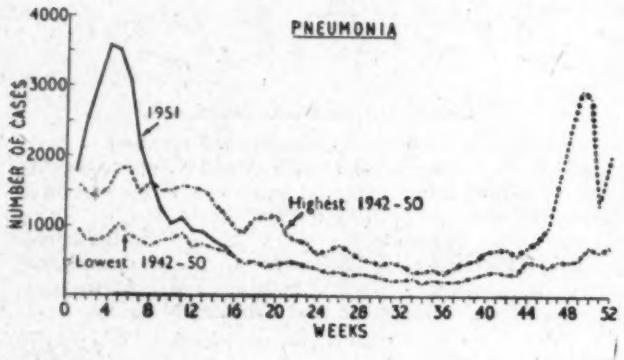
Graphs of Infectious Diseases

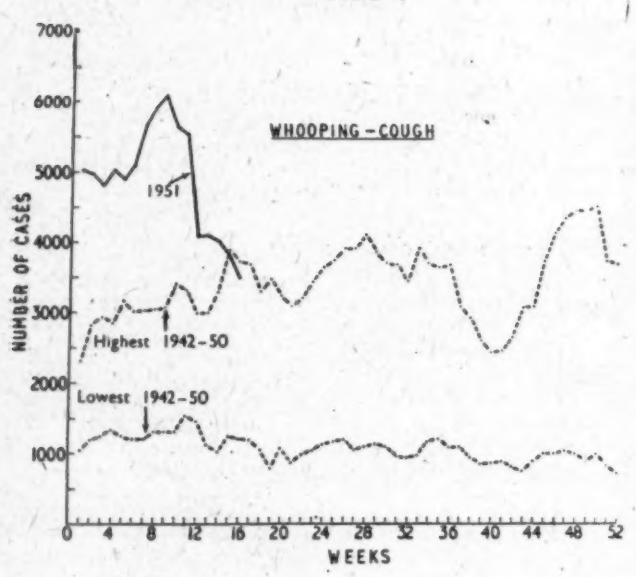
The graphs below show the uncorrected numbers of cases (deaths from influenza) of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus -------, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.

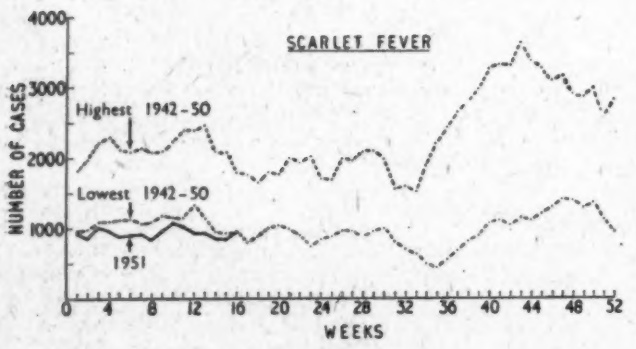












Week Ending April 28

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,084, whooping-cough 3,643, diphtheria 32, measles 18,006, acute pneumonia 570, acute poliomyelitis 19, dysentery 871, paratyphoid fever 4, typhoid fever 4. Deaths from influenza in the great towns numbered 13.

Medical News

International Code of Medical Ethics

One of the first actions of the World Medical Association, whose Council has just been meeting in Geneva, was to draw up an International Code of Ethics. This was in effect an addendum to "The Declaration of Geneva," a modern form of the Hippocratic oath to be taken by the newly qualified doctor, formulated by the W.M.A. in September, 1948. These two texts are reproduced in the April issue of *World Medical Association Bulletin*. Any doctor wishing to obtain copies of the code and the declaration, handsomely printed on fine vellum stock, may obtain them free of charge on application to Abbott Laboratories, North Chicago, Illinois, U.S.A.

Centenary of Royal Cancer Hospital

The Royal Cancer Hospital, which this month celebrates its centenary, owes its foundation to the efforts of Dr. William Marsden (1796–1867), who had previously opened the Royal Free Hospital in 1828. In February, 1851, he called a meeting of influential people, and three months later the Free Cancer Hospital was opened, at first for out-patients only. Six beds were provided in June, 1852, and four months later an additional in-patient department was opened in West Brompton. The necessity for still further accommodation led in 1856 to the purchase of the present site in Fulham Road. The foundation stone was laid in 1859 and the first patient admitted on January 10, 1862. To-day it is a school of the University of London, with chairs of radiology, experimental pathology, and chemistry. In addition to undergraduate teaching, post-graduate instruction in experimental pathology and radiology has been given since 1931. The hospital will be open to visitors from May 15 to 18, and the Chester Beatty Research Institute on May 16 from 7 p.m. to 9 p.m. and May 17 from 10 a.m. to 6 p.m., when a series of demonstrations will be presented. A detailed programme may be obtained from the House Governor at the hospital.

North of England Obstetrical and Gynaecological Society

An extraordinary general meeting of the society was held in Leeds on April 27, with the president, Dr. J. W. A. Hunter, in the chair. Mr. David Currie read a paper and showed a film on an operation for the cure of a prolapsed vault, and Mr. P. Malpas and Dr. J. C. Brundet reported a case of haemangioma of the uterus.

Scottish Society of Anaesthetists

The annual meeting was held at Dunblane Hydro, Perthshire, April 27–29. The president, Dr. H. H. Pinkerton, Glasgow, delivered his address on "General Anaesthesia for Collapse Therapy in Pulmonary Tuberculosis." Dr. T. J. C. MacDonald, Aberdeen, was elected vice-president for the ensuing year. Dr. W. W. Mushin was a guest of the society, and gave a short talk which he entitled, "The Null Hypothesis." The prize which the society is awarding annually for the best paper submitted from a registrar was won by Dr. J. G. Robson, Glasgow, who read a résumé of his paper. A company of 110, comprising members, their wives, and guests, was present at dinner on Saturday evening.

Society of Chiropodists Dinner

The annual dinner was held in London on April 26 with the president, Mr. John H. Hanby, in the chair. The society's health was proposed by Mr. H. Osmond-Clarke, who referred to his long association with the profession in Manchester and emphasized the links between chiropody and orthopaedics. In his reply the president mentioned the help and guidance they had received since 1912 from medical men, in particular Mr. Norman C. Lake, and their future under the Cope report. The Dean of St. Paul's (the Very Reverend Dr. W. R. Matthews) proposed the health of the medical profession and praised the family doctor, to so many a guide, philosopher, and friend. Lord Webb-Johnson, in a humorous reply, spoke of the value of having one society to represent the whole profession, both in and out of the Health Service, and asked whether a better term than "medical auxiliary" could not be found.

Society for General Microbiology

Professor J. W. McLeod has been appointed president of the Society for 1951–2, and Dr. J. G. Davis general secretary. The Society, which was founded in 1945, now has 985 members and will hold its September meeting at Manchester. Information about the Society may be obtained from the general secretary, 35, Villiers Road, Southall, Middlesex.

Chaplains in Hospital

The Ministry of Health has reminded hospital management committees that they should provide for the spiritual needs of patients and staff by setting aside a room or chapel (which may be dedicated, but not consecrated—or it cannot be used interdenominationally) and appointing chaplains. A whole-time chaplain may be appointed where there are 750 patients of his denomination, and he is then, in general, to be treated like other hospital officers in matters of leave, pension, etc. Regional boards are advised to set up special committees for Anglican appointments, after consulting the bishops of the dioceses concerned. Roman Catholic and Free Church appointments should be made in direct agreement with their religious authorities.

Foreign Women for Hospitals

The Ministry of Labour has arranged with the German Federal Department of Labour to put British employers who want to engage German women for resident domestic work in hospitals in touch with German women who wish to take up this work. They may also be employed or trained as student nurses in recognized training hospitals, as nursing assistants in mental hospitals, or as nursing orderlies in all types of hospitals and nursing-homes. Full particulars and forms of application for domestic workers may be obtained from local labour exchanges; for nursing staff application should be made to the Nursing Appointments Offices of the Ministry.

Rehabilitation of Children

The two-months team-training course on the rehabilitation of physically handicapped children (*British Medical Journal*, March 10, p. 539) has just completed its work. The programme and syllabus of the course were prepared by Dr. Harold Balme, and the general medical lectures were given by Sir Allen Daley, Drs. Wilfrid Sheldon, C. D. S. Agassiz, F. S. Cooksey, and Evelyn Lucas. During the first fortnight an attempt was made to present a complete picture of modern treatment, rehabilitation, education, vocational training, and employment of physically handicapped children and disabled young workers. This was accomplished partly by a series of lectures and films, and partly by visits to orthopaedic hospitals for children, special schools, training institutions, and employment agencies. One whole day during this period was devoted to a study of the school medical service. Four weeks of the course were spent in intensive technical training, the teams being broken up into groups according to their various specialties. The final week was devoted to reports from the students themselves. This is the first time that an attempt has been made to plan a training course on team lines in the field of rehabilitation, and its success should encourage similar attempts in the future.

Wills

Dr. William Hugh Steele, of Newton Abbot, Devon, a pioneer in radiography, who took the first *x*-ray apparatus to the relief of Ladysmith in the Boer War, and who was radiologist to Newton Abbot Hospital, left £25,286; among other bequests he left:

£100 to the Royal Medical Benevolent Fund General Fund and £200 for the Christmas Gifts Fund, £150 to the R.A.F. Benevolent Fund, £50 each to the British Sailors Society, the Training Ship *Arethusa*, the Old War Horse Memorial Hospital Fund, and the Royal Medical Foundation of Epsom College, £200 to the Royal Beneficent Association, and by a codicil dated August 16, 1949, he revoked a legacy of £3,000 to the Newton Abbot Hospital and Dispensary "as the said hospital is now maintained by the State," and he left the balance of his property to the Royal Medical Benevolent Fund, for the General Fund of that Institution.

Dr. Haigooni Dikran Absalom Utidjian, of Kenton, Middlesex, formerly of Nicosia, Cyprus, left £21,567, including £100 to the Armenian National Hospital at Yedi Koule, Constantinople.

COMING EVENTS

Festival Lecture

The title of the Festival Lecture, which Sir Henry Dale will give at 6.30 p.m. on June 20 in the Great Hall of B.M.A. House, Tavistock Square, London, W.C.1, will be "Medicine Yesterday and To-morrow." Admission will be by ticket, obtainable from the Public Relations Officer, B.M.A. House.

Conference on Ageing

The British Society for Research on Ageing will hold its annual conference on June 2, at 3 p.m., at the Medical School of the Middlesex Hospital, London, W.1. The agenda can be had from the Secretary of the Society, Dr. V. Korenchevsky, Department of Physiology, Oxford.

International Scientific Film Association

The fifth congress of the International Scientific Film Association is to be held at The Hague, in the Municipal Museum, from September 15 to 22. During this period there will be meetings of the permanent committees dealing with medical, research, technical, and industrial films, and a special committee of the British Scientific Film Association will be set up to consider films for the Scientific Film Festival. Information about the association may be had from the secretary, the Scientific Film Association, 4, Great Russell Street, London, W.C.1.

Manchester Golf Competition

The Manchester and District Medical Golfers' Association will hold its annual competition at Mere on May 23. Any medical man is eligible for membership provided he is a member of a recognized golf club within the area, and all inquiries should be addressed to the hon. secretaries, Manchester and District Medical Golfers' Association, c/o B.M.A. Regional Office, 33, Cross Street, Manchester, 2. Telephone: Deansgate 3691.

Service Reunion

106(Br) General Hospital reunion dinner and dance will be held on Saturday, May 26, at 261, South Lambeth Road, S.W.8. Tickets from W. Gwynn-Jones, 23, Keyes Road, Cricklewood, N.W.2. Telephone: GLAdstone 1141.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday

EDINBURGH UNIVERSITY.—At Physiology Class Room, May 14, 5 p.m., *"The Mediaeval Conception,"* by Dr. Douglas Guthrie.

Tuesday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 15, 5 p.m., *"Bonds and Blisters, The Physics and Chemistry of Blister Formations,"* by Dr. E. J. Moynahan.

ST. MARY'S HOSPITAL MEDICAL SCHOOL: WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, Paddington, London, W.—May 15, 5 p.m., *"The Problem of Protection Against Staphylococcal Infections,"* Almroth Wright Lecture by Professor Wilson Smith, F.R.S.

Wednesday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 16, 5 p.m., *"Chronic Inflammation,"* by Dr. J. O. Oliver.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—May 16, 5.30 p.m., *"How Far Do Fundus Appearances Reflect Cardiovascular Diseases?"* by Dr. C. J. Gavey.

NORTH-EAST LONDON MEDICAL SOCIETY.—At Prince of Wales's Hospital, London, N., May 16, 3.30 p.m., clinical meeting.

OXFORD UNIVERSITY.—At Radcliffe Infirmary, Oxford, May 16, 5 p.m., *"Defences of the Air Passages, With Relation to Ciliary Action,"* Litchfield Lecture by Mr. V. E. Negus.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—May 16, 5 p.m., *"Professional Freedom,"* Croonian Lecture by Dr. T. Fortescue Fox.

UNIVERSITY COLLEGE, Physiology Theatre, Gower Street, London, W.C.—May 16, 5.30 p.m., *"Studies in Comparative Electrophysiology,"* by Professor A. Fessard (Collège de France).

Thursday

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, London, W.—May 17, (1) 8.15 p.m., annual general meeting; (2) 8.45 p.m., *"The Influence of Radiology on the Diagnosis and Treatment of Intrinsic Carcinoma of the Larynx,"* 28th Mackenzie Davidson Memorial Lecture by Sir Stanford Cade.

EDINBURGH UNIVERSITY, University New Buildings (Anatomy Theatre), Teviot Place, Edinburgh.—May 17, 5 p.m., *"Arteriovenous Malformations of the Head,"* Honyman Gillespie Lecture by Mr. John Gillingham.

MIDDLESEX COUNTY MEDICAL SOCIETY.—At Napsbury Hospital, near St. Albans, Herts, May 17, 3 p.m., *"Transorbital Leucotomy,"* coloured film.

OXFORD UNIVERSITY.—At Radcliffe Infirmary, Oxford, May 17, 4.15 p.m., *"Incoordinate Uterine Action,"* Litchfield Lecture by Professor T. N. A. Jeffcoate.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At 26, Portland Place, London, W., May 17, 7.30 p.m., *"Pathological Processes in Malaria: Progress Report,"* by Professor Brian Maegraith, Dr. E. Sherwood Jones, and Dr. W. H. H. Andrews. A discussion will follow.

ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, May 17, 5 p.m., *"Physiological and Clinical Importance of Noradrenaline,"* by Professor J. H. Burn.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—May 17, 4.30 p.m., *"Psychiatry,"* lecture-demonstration by Dr. Desmond Curran.

UNIVERSITY COLLEGE, Physiology Theatre, Gower Street, London, W.C.—May 17, 4.45 p.m., *"Energy Transformations in Living Matter,"* by Professor H. A. Krebs.

Friday

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, London, W.—May 18, 5 p.m., meeting of medical members.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., May 18, 2.15 p.m., *"The Meningiomas,"* Skinner Lecture by Sir Geoffrey Jefferson, F.R.S.

INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 18, 5.30 p.m., clinical demonstration by Dr. G. B. Dowling.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—May 18, 5.30 p.m., *"Gonioscopy After Glaucoma Operations,"* by Mr. H. E. Hobbs.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—May 18, 5 p.m., *"Ophthalmic Injuries,"* by Miss M. Savory.

UNIVERSITY COLLEGE, Physiology Theatre, Gower Street, London, W.C.—May 18, 5.30 p.m., *"Natural and Synthetic Sympatholytic Drugs, and Their Structural Relationship with Sympathomimetic Substances,"* by Professor D. Bovet (Rome).

Saturday

SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Preston Hall, near Maidstone, May 19, 10.30 for 11 a.m., *"In My Opinion,"* by Dr. H. V. Morlock.

APPOINTMENTS

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—*Part-time Consultant Radiologist, St. Margaret's Hospital, Epping,* F. Bush, M.B., B.Chir., D.M.R.E. *Part-time Consultant Orthopaedic Surgeon, Colchester Group of Hospitals,* D. M. Dunn, F.R.C.S.Ed. *Full-time Consultant Area Pathologist, Prince of Wales Hospital,* W. I. Leslie, M.B., Ch.B. *Full-time Consultant Pathologist, Leytonstone Group of Hospitals,* C. Raeburn, M.R.C.S., L.R.C.P.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—*Deputy Director of Regional Blood Transfusion Service,* N. F. W. Brueton, M.B., Ch.B. *Senior Medical Registrar, Bath Clinical Area,* D. J. Ellison, M.B., Ch.B., M.R.C.P.Ed. *Registrar in Thoracic Surgery, Hawkmoor Sanatorium, Bovey Tracey,* L. E. Neri, M.B., B.S. *Assistant Pathologist, Frenchay Hospital,* J. G. C. Spencer, M.D., F.R.C.S. *Consultant Surgeon to South Somerset Clinical Area (Minehead District),* G. H. Darke, M.B., B.S. *Senior Registrar in Psychiatry, Bristol Mental Hospitals,* B. V. Earle, M.D., M.R.C.P.

TYSER, P. A., M.D., D.P.H., Medical Officer of Health, Cambridgeshire Rural Districts, and Deputy County Medical Officer of Health and School Medical Officer, Cambridgeshire County Council.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Barkworth.—On April 28, 1951, to Beryl (formerly Wright), wife of Dr. F. B. S. Barkworth, of Oakhampstead, Dittons Road, Eastbourne, a brother for Paul and John—Peter Mark Reginald.

Barwise.—On April 8, 1951, at Plymouth, to Dr. Maureen Barwise (formerly Bassett), wife of Dr. David Barwise, a daughter—Susan Mary.

Ferguson.—On May 4, 1951, at the Shearwood Nursing Home, Sheffield, to Brenda, wife of Dr. Malcolm Ferguson, a son—Clive Anthony.

Friedlander.—On May 2, 1951, at Doris Court, Manchester, to Dr. Jean L. Broughton, wife of Dr. H. A. Friedlander, a daughter.

Hall-Smith.—On April 30, 1951, at 61, The Drive, Hove, to Angela, wife of Dr. Patrick Hall-Smith, a daughter.

Harris.—On May 2, 1951, to Dorothy (formerly Kennedy), wife of Dr. R. Vincent Harris, of 6, College Road, Eastbourne, Sussex, a daughter—Joan Pamela.

Lawrence.—On May 4, 1951, at the City Hospital, Derby, to Bronwen (formerly Arthur), wife of Dr. Ralph A. A. R. Lawrence, of the Derbyshire Royal Infirmary, a son.

Little.—On May 2, 1951, at Chertsey Hill Nursing Home, Carlisle, to Catherine (formerly Salt), wife of Dr. J. C. Little, a daughter—Edith Alison.

Martin.—On April 28, 1951, at the Queen Elizabeth Hospital, Birmingham, to Winifred (formerly Attenborough), wife of Dr. Robert F. Martin, a daughter—Patricia Catherine.

Templeman.—On April 10, 1951, at the Fallodon Nursing Home, Leeds, to Anne, wife of Dr. G. H. Templeman, M.B.E., M.D., a brother for Susan Joy—John.

DEATHS

De Penning.—On February 13, 1951, Herbert Clement De Penning, M.R.C.S., L.R.C.P., of 38, Milton Road, Portsmouth, aged 68.

Dunlop.—On May 2, 1951, at Lake Cottage, Sandhead, Stranraer, James Dunlop, L.R.C.P.&S.Ed., L.R.F.P.S., D.P.H.

Hamlett.—On March 21, 1951, at Winsford, Cheshire, Constance Clara Maude Hamlett, M.R.C.S., L.R.C.P., aged 52.

Henderson.—On April 30, 1951, at General Hospital, Birmingham, Elizabeth Eleanor Henderson (formerly Benson), M.B., Ch.B., D.P.H., of Redditch, Worcs.

Lamballe.—On May 5, 1951, at 82, Millfield Lane, York, Frederic William Lamballe, M.B., B.S., Lieutenant-Colonel, R.A.M.C., ret.

Livingstone-Learmonth.—On April 28, 1951, at Edinburgh, Basil Lockhart Livingstone-Learmonth, M.B., C.M., late of Peking, China, and Plockton, Ross-shire, aged 84.

Miller.—On April 30, 1951, at Bradford Royal Infirmary, Christopher Graham Miller, B.M., B.Ch., of Harrogate, Yorks, aged 24.

Simson.—On May 6, 1951, at 217, Wilton Road, Southampton, Henry John Simson, M.B., Ch.B., D.P.H.

Stephen.—On May 2, 1951, at 35, South Hill Park, London, N.W., George Mackie Stephen, M.B., Ch.B.

Stevenson.—On April 9, 1951, at Sheffield, Eliza Moira Kennedy, M.D., F.R.F.P.S., of 1, Kingsborough Gardens, Glasgow, W.

Theobalds.—On May 1, 1951, at 9, Lancaster Grove, London, N.W., Owen Le Mare Theobalds, M.R.C.S., L.R.C.P., aged 90.

Trapnell.—On April 28, 1951, at 58, Manor Way, Beckenham, Kent, Francis Cyril Trapnell, M.D.

Walters.—On April 21, 1951, at Longburgh, near Carlisle, Arthur Piercefield Walters, M.R.C.S., L.R.C.P., aged 87.

Wayte.—On May 4, 1951, at a Croydon nursing-home, John Wayte, M.B., B.Ch., of 33, Chatsworth Road, Croydon, aged 89.

Yearsley.—On May 4, 1951, at "Winscombe," Gerrard's Cross, Bucks, Percival Macleod Yearsley, F.R.C.S., aged 83.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Nitrogen Mustards in Glomerulo-nephritis

Q.—*I have a patient who developed nephritis during pregnancy a year ago and has not improved after medical treatment along the usual lines. Would treatment with nitrogen mustard be indicated? Secondly, does decapsulation and/or denervation of the kidney help at any stage of nephritis?*

A.—There is reason to believe that diffuse glomerulonephritis may result from immunological alteration in renal tissue. Since nitrogen mustard is known to prevent the development of certain immunological reactions, Chasis, Goldring, and Baldwin (*Proc. Soc. exp. Biol., N.Y.*, 1949, **71**, 565) tried its effect in nephritis. They administered methyl-*bis* (β-chloroethyl) amine hydrochloride intravenously to three patients in the nephrotic stage of the illness, in two doses of 0.2 mg. per kilo of body weight on successive days. In one patient on two separate occasions this was followed by diuresis and a diminution in proteinuria. In a subsequent note (*J. clin. Invest.*, 1950, **29**, 804) they report on its administration to eight patients with glomerulo-nephritis. At the time of the report two had died, three were still under treatment, and three were strikingly improved for periods lasting up to eight months. This treatment should still be regarded as experimental. Its efficacy has not yet been proved with certainty, for any form of therapy is difficult to assess in a disease which is so variable in its course.

There is no evidence that decapsulation and/or denervation of the kidney help at any stage of nephritis.

Tallqvist Method of Haemoglobinometry

Q.—*How useful is Tallqvist's method of estimating haemoglobin?*

A.—The Tallqvist method is a useful procedure for the approximate estimation of haemoglobin. The principal objection to the method is that the standards consist of a series of definite increments, so that one must guess at intermediate values. A drop of blood on blotting-paper is compared with lithographed paper standards (Wireless Printing Co., New York) and the standard is selected which most nearly matches the spot. Although seemingly a somewhat crude procedure, the Tallqvist has yielded results which are of about the same accuracy as those obtainable with most dilution haemoglobinometers, such as the Haldane and Sahli.

Macfarlane, King, Wootton, and Gilchrist (*Lancet*, 1948, **1**, 282) found the Tallqvist method capable of yielding results only slightly inferior to the Haldane method. Their "error quantities" chart shows that a single observer should be able to determine differences in haemoglobin concentration of about 2 g./100 ml., corresponding to about 12%, on the blood of normal individuals. By the Haldane method the corresponding figures are about 1.6 g. haemoglobin, equivalent to about 9%. The coefficients of variation for a large group of observers in Oxford were 9.7% for the Tallqvist method and 9.0% for Haldane. On the other hand, the accuracy attainable by photo-electric and photometric methods and by the Medical Research Council grey wedge photometer is much better than this; these corresponded to only a few-per-cent error (3–5 at the most), and showed a coefficient of variation of only 1–2% with a group of observers (King *et al.*, *Lancet*, 1948, **2**, 563 and 971).

Jerusalem Artichokes

Q.—*Are Jerusalem artichokes indigestible? I understand that they are excreted unchanged.*

A.—The most prominent constituent of the Jerusalem artichoke is inulin, a carbohydrate which is made up of fructose units in the same way as starch is made up of glucose units. Inulin may be absorbed into the system, but no enzymes are available to break it down into fructose. It is therefore excreted in unchanged form by the kidneys, and has indeed been used in kidney function tests. One authority holds the view that inulin may to some extent be broken down by the intestinal bacteria into fatty acids, which can be absorbed and utilized as a source of energy.

Asthma and Horses

Q.—*A patient aged 25, the daughter of a trainer, spends her life handling racehorses. For the past two years she has suffered from attacks of asthma after their evening grooming, though she worked for two or three years previously with impunity. She gives no previous history of chest trouble or allergic disorder. The asthma seems strictly related to contact with horses, and I do not think anxiety is a factor, since she is comparatively free of the asthma provided she limits herself to riding and the morning grooming only. She has been treated with a full course of an extract of horse dander, but without improvement. The attacks are largely prevented by ephedrine and "benadryl" given early, but she wishes to acquire a more permanent immunity if possible. What treatment do you recommend?*

A.—It is first of all essential to confirm that sensitivity to horse dander is the cause of the patient's asthma. It is surprising that she has no symptoms during the morning grooming, but only when doing the same thing at night. Furthermore, if she were sensitive to horse dander one would expect definite improvement following the desensitizing injections. Does she give positive skin tests to horse dander extract?

Has the possibility of sensitization to other atopens with which she might come into contact during the evening grooming been considered? For example, feeding materials such as bran or oats might be responsible. If sensitivity to horses can be definitely confirmed, a stronger extract of horse dander could be used and might produce a more favourable response.

Histamine Poisoning after Antihistamine Drug

Q.—*A woman aged 35 recently took two tablets of an antihistamine compound for an urticarial rash on the face. In a short time she had severe abdominal pains of sudden onset, sweating, flushing, malaise, and aching in the back and calves. The symptoms disappeared within 12 hours. Is this a typical picture of poisoning by these drugs?*

A.—The symptoms caused in this patient are very unusual, for the usual symptoms of poisoning with antihistamine compounds are those of cerebral depression.

The symptoms are much more like those due to histamine itself, and it is conceivable that the drug acted not by antagonizing the effect of histamine in the body but by potentiating it. Antihistamine compounds are known to have some potentiating action on the production of acid gastric juice by histamine, and it is therefore not unlikely that occasionally they will be found to fail in their normal antagonistic action in other directions.

Patients vary a good deal in their response to different antihistamine substances, and the patient in question would probably respond differently to another compound of the same class. It would be interesting to know whether this patient had already been taking antihistamine compounds for a long time.

Kyphoscoliosis and Pulmonary Hypertension

Q.—*What is the mechanism by which kyphoscoliosis gives rise to pulmonary hypertension?*

A.—Kyphoscoliosis when severe causes a combination of collapse atrophy of part of the lung and over-expansion of the remainder. The over-expanded lung becomes emphysematous, and in time the patient comes to suffer from pulmonary heart disease indistinguishable from that associated with ordinary severe emphysema. This hypertension is generally attributed to gross limitation of the total cross-section of the pulmonary capillaries, so that the pulmonary blood pressure rises steeply on effort. Secondary changes in the small pulmonary arteries and arterioles may help to cause chronic pulmonary hypertension, and during acute infection increased anoxia temporarily lifts the blood pressure even higher. Finally, a compensatory increase of cardiac output occurs in most of these cases, and this aggravates the hypertensive effect of the diminished cross-section of the peripheral pulmonary vessels.

Trauma and Local Lesions of Syphilis

Q.—*Will trauma to a syphilitic person predispose to the development of a local lesion? For instance, (a) would a knock on the skin predispose to a syphilitic periostitis, or (b) would the removal of a foreign body from the eye predispose to the development of interstitial keratitis in that eye?*

A.—There is much evidence, both clinical and experimental, that trauma to a patient suffering from syphilis (usually latent or tertiary, rarely secondary) predisposes to the localization of lesions. Good examples are the appearance of gummata in tattoo marks and palmar syphilides in labourers. The effects of heat on the faces of cooks and on the arms of washerwomen also predispose to rashes in these areas. It should also be noted that the formation of condylomata lata during the secondary phase of the disease is partly due to friction.

The answers to the specific queries contained in the question are (*a*) yes, and (*b*) yes, but only in the congenital form of the disease. Interstitial keratitis in acquired syphilis is extremely rare, and the trauma of the removal of a foreign body would more likely predispose to the formation of a gumma. Many cases of interstitial keratitis in congenital syphilitics have been reported (some with interesting medico-legal implications) as having been precipitated by trauma, not only to the eye itself but also to adjacent tissues.

Pituitary Dyscrasia in Children

Q.—*What are the causes, treatment, and prognosis of pituitary dyscrasia in infants and young children? Have vitamin preparations any place in its treatment?*

A.—This is too large a question to deal with briefly unless one interprets it as asking what effects on the pituitary gland can non-endocrine illness have in infants and children. Histologically, Lorain in 1871 (after whom the infantilism syndrome of Levi–Lorain is named) put forward the conception of infantilism in a preface to an article by one of his pupils entitled "Du féminisme et de l'infantilisme chez les tuberculeux." This drew attention to the fact that failure of somatic and sexual development could occur as the result of chronic tuberculosis in childhood, and when Levi, in 1908, drew attention to the pituitary origin of infantilism the two ideas linked up. Any chronic illness in childhood—for example, syphilis, tuberculosis, malaria, pancreatic disease, coeliac disease—may have similar endocrine results. Since lack of growth and sexual development may also occur with chronic malnutrition this factor would appear to play a part. However, the use of vitamins would only be justified in this type of infantilism where primary or secondary malnutrition was operative.

Effect of Carbon Monoxide on Vision

Q.—*A man working on the gas mains was overcome by gas, which is composed of a mixture of carburetted water gas and coal gas. His central vision was not affected, but he has a homonymous hemianopia. It is now three months since the accident, and there is very little improvement in the fields of vision. What is the prognosis, and are there any references on the subject?*

A.—Carburetted water gas is made by passing steam over red hot coke, hydrogen and carbon monoxide being given off and injected with gas oil. Thus the effects of inhaling a mixture of C.W.G. and coal gas are those of acute carbon monoxide poisoning. As there is very little improvement in the fields of vision after three months in the case in question the damage is likely to be permanent. The literature on carbon monoxide asphyxia contains a fair number of reports of permanent damage to vision (e.g., Drinker's *Carbon Monoxide Asphyxia*, 1938, London).

Discharging Tuberculous Sinus

Q.—*A child (3 years) has a discharging sinus from tuberculous glands in the neck: the sinus has now been discharging for about six weeks. What is the best line of treatment? Would penicillin injections with sulphonamides by mouth help to clear up the condition?*

A.—In the majority of cases of tuberculous infection of the cervical glands microscopical examination of the tonsils and adenoids will show gross infection with tubercle bacilli in either or both. Guinea-pig inoculation gives an even higher percentage of positive results. This infection may, but often does not, accompany the ordinary "T. & A." catarrhal infections. In consequence, to remove and examine the tonsils and adenoids as a first step in treating tuberculous glands of the neck in children is a rule to many surgeons of large experience. They must be expertly removed by dissection; the guillotine is quite unreliable at this age. The discharge is caused by the necrotic mass of tuberculous gland tissue at the bottom of the sinus, and will continue as long as the necrotic tissue remains. Penicillin and sulphonamides, therefore, will have no influence at all on the process. When all the tuberculous tissue has dissolved, the discharge, which may have appeared as if it would continue indefinitely, suddenly ceases. Hence this condition supplies many miraculous cures, the agents varying from osteopathy to Abrams's box and visits to favoured localities for sea-air or even less tangible benefits.

No surgeon of experience will lightly undertake a complete excision of the infected mass in such a case as this, but healing can be much accelerated by expressing the necrotic tissue by strong pressure upon it, applied through a piece of gauze at the time of the tonsillectomy and repeated until no more fine fragments can be forced out of the sinus. Curettage is unreliable owing to the impossibility of knowing where the necrotic tissue lies.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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